```
=> D HIS FUL

     FILE 'REGISTRY' ENTERED AT 09:43:58 ON 27 DEC 2007
L56             STR
L58          336 SEA SSS FUL L56
L59             STR
L60          145 SEA SUB=L58 SSS FUL L59
L61             STR
L63             SCREEN 2127
L64           33 SEA SUB=L58 SSS FUL L61 NOT L63

     FILE 'HCAPLUS' ENTERED AT 09:50:37 ON 27 DEC 2007
L65         3561 SEA ABB=ON  PLU=ON  L64

     FILE 'REGISTRY' ENTERED AT 09:50:43 ON 27 DEC 2007
L66            1 SEA ABB=ON  PLU=ON  "MEVINOLINIC ACID"/CN

     FILE 'HCAPLUS' ENTERED AT 09:53:45 ON 27 DEC 2007

     FILE 'REGISTRY' ENTERED AT 09:54:07 ON 27 DEC 2007
                SET SMARTSELECT ON
L67             SEL PLU=ON  L66 1- CHEM :      10 TERMS
                SET SMARTSELECT OFF

     FILE 'HCAPLUS' ENTERED AT 09:59:08 ON 27 DEC 2007
L68          162 SEA ABB=ON  PLU=ON  L67
L69          164 SEA ABB=ON  PLU=ON  L68 OR MEVINOLINIC(W)ACID OR MEVINOLINATE
L70          119 SEA ABB=ON  PLU=ON  L65 AND L69
L71        18338 SEA ABB=ON  PLU=ON  ("FERMENTATION (L) BROTH"/CV OR "BROTH
                FERMENTATION"/CV) OR FERMENTATION(L)(BROTH OR MEDIA)
L72           13 SEA ABB=ON  PLU=ON  L69(L)L71
L74          328 SEA ABB=ON  PLU=ON  L65(L)(BMF OR PREP OR BPN)/RL
L75           30 SEA ABB=ON  PLU=ON  L70 AND L74
                D STAT QUE L75
                D IBIB ABS HITSTR L75 1-30
L76         8124 SEA ABB=ON  PLU=ON  LACTONIZATION/CV OR ?LACTONIZATION OR
                ?LACTONISATION

     FILE 'REGISTRY' ENTERED AT 10:01:56 ON 27 DEC 2007
L79           18 SEA ABB=ON  PLU=ON  MINERAL(L)ACID OR SULFONIC ACID/CN OR
                NITRIC ACID/CN OR ORTHOPHOSPHORIC ACID/CN OR HYDROCHLORIC
                ACID/CN

     FILE 'HCAPLUS' ENTERED AT 10:03:12 ON 27 DEC 2007
                S L79 OR (MINERAL OR SULFURIC OR NITRIC OR ORTHOPHOSPHORIC ACID

     FILE 'REGISTRY' ENTERED AT 10:04:03 ON 27 DEC 2007
L80            1 SEA ABB=ON  PLU=ON  ORTHOPHOSPHORIC ACID/CN

     FILE 'HCAPLUS' ENTERED AT 10:04:03 ON 27 DEC 2007
L81        72933 SEA ABB=ON  PLU=ON  L80
L82       399316 SEA ABB=ON  PLU=ON  L79 OR (MINERAL OR SULFURIC OR NITRIC OR
                L81 OR HYDROCHLORIC)(W) ACID
L83           15 SEA ABB=ON  PLU=ON  L74 AND L82

     FILE 'REGISTRY' ENTERED AT 10:05:29 ON 27 DEC 2007
L84         1388 SEA ABB=ON  PLU=ON  SOLVENT OR SOLVENTS OR HYDROCARBONS/CN
```

```
     FILE 'HCAPLUS' ENTERED AT 10:10:13 ON 27 DEC 2007
L86     1959522 SEA ABB=ON  PLU=ON  L83 OR L84 OR SOLVENT OR HYDROCARBON OR
                ?DICHLOROMETHANE OR CHLOROFORM OR ISOPROPANOL OR ALUMINA OR
                ACETONE
L87         233 SEA ABB=ON  PLU=ON  L65 AND L86
L88          48 SEA ABB=ON  PLU=ON  L87 AND L74
L89          80 SEA ABB=ON  PLU=ON  L65 AND (FILT? OR ?CRYSTALI? OR EVAPORA?)
L90          29 SEA ABB=ON  PLU=ON  L89 AND L74
L91          45 SEA ABB=ON  PLU=ON  (L83 OR L88 OR L90) NOT L75
                D STAT QUE L91
                D IBIB ABS HITSTR L91 1-45

     FILE 'REGISTRY' ENTERED AT 10:28:41 ON 27 DEC 2007
L92         112 SEA ABB=ON  PLU=ON  L60 NOT L64
L93         133 SEA ABB=ON  PLU=ON  L92 OR LOVASTATIN

     FILE 'HCAPLUS' ENTERED AT 10:29:16 ON 27 DEC 2007
L94        6902 SEA ABB=ON  PLU=ON  L93 OR LOVASTATIN
L95         462 SEA ABB=ON  PLU=ON  L94(L)(BMF OR PREP OR BPN)/RL
L97          60 SEA ABB=ON  PLU=ON  L95 AND L69
L98          23 SEA ABB=ON  PLU=ON  L97 AND L86
L99          10 SEA ABB=ON  PLU=ON  L98 NOT (L75 OR L91)
                D STAT QUE L99
                D IBIB ABS HITSTR L99 1-10
L100          3 SEA ABB=ON  PLU=ON  L72 NOT (L75 OR L91 OR L99)
                D STAT QUE L100
                D IBIB ABS HITSTR L100 1-3
L101        458 SEA ABB=ON  PLU=ON  ("KUMAR SANJAY"/AU OR "KUMAR SANJAY
                RAI"/AU OR "KUMAR SANJAY S"/AU OR "KUMAR SANJAY SANTH"/AU) OR
                VAISHNAV SANJAY KUMAR/AU
L102         13 SEA ABB=ON  PLU=ON  THAKUR B/AU OR THAKUR BHUPENDRA HARISHCHAND
                RA/AU
L103         10 SEA ABB=ON  PLU=ON  KADAM S/AU OR KADAM S R/AU OR KADAM
                SUBHASH R?/AU
L104          1 SEA ABB=ON  PLU=ON  L101 AND (L102 OR L103)
L105          1 SEA ABB=ON  PLU=ON  L102 AND L103
L106          3 SEA ABB=ON  PLU=ON  (L101 OR L102 OR L103) AND (L65 OR L68 OR
                L71 OR L76 OR L94)
L107          2 SEA ABB=ON  PLU=ON  (L104 OR L105 OR L106) NOT (L75 OR L91 OR
                L99)
                D STAT QUE L107
                D IBIB ABS HITSTR L107 1-2


     FILE HOME

     FILE REGISTRY
     Property values tagged with IC are from the ZIC/VINITI data file
     provided by InfoChem.

     STRUCTURE FILE UPDATES:   26 DEC 2007  HIGHEST RN 959588-76-2
     DICTIONARY FILE UPDATES:  26 DEC 2007  HIGHEST RN 959588-76-2

     New CAS Information Use Policies, enter HELP USAGETERMS for details.

     TSCA INFORMATION NOW CURRENT THROUGH June 29, 2007
```

Please note that search-term pricing does apply when conducting SmartSELECT searches.

REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

http://www.cas.org/support/stngen/stndoc/properties.html

FILE HCAPLUS

FILE COVERS 1907 - 27 Dec 2007 VOL 147 ISS 26
FILE LAST UPDATED: 26 Dec 2007 (20071226/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

=>
=> FIL HCAPLUS
FILE 'HCAPLUS' ENTERED AT 09:59:08 ON 27 DEC 2007
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

Copyright of the articles to which records in this database refer is held by the publishers listed in the PUBLISHER (PB) field (available for records published or updated in Chemical Abstracts after December 26, 1996), unless otherwise indicated in the original publications. The CA Lexicon is the copyrighted intellectual property of the the American Chemical Society and is provided to assist you in searching databases on STN. Any dissemination, distribution, copying, or storing of this information, without the prior written consent of CAS, is strictly prohibited.

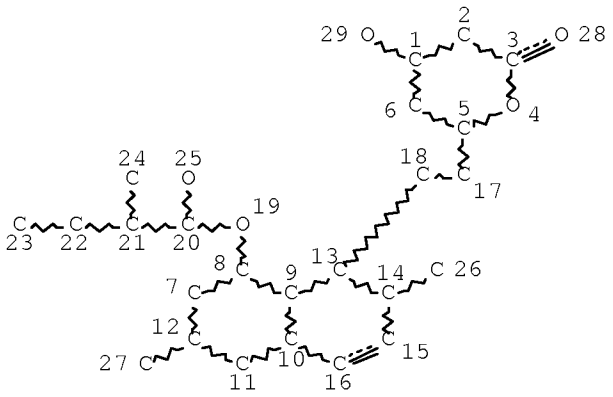
FILE COVERS 1907 - 27 Dec 2007 VOL 147 ISS 26
FILE LAST UPDATED: 26 Dec 2007 (20071226/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

=>
=>

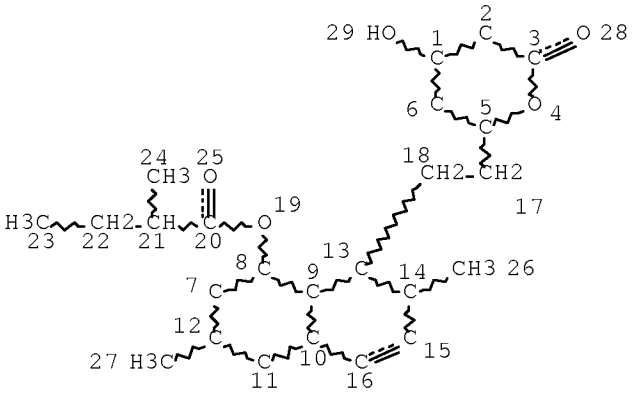
=> D STAT QUE L75
L56 STR



NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 29

STEREO ATTRIBUTES: NONE
L58 336 SEA FILE=REGISTRY SSS FUL L56
L61 STR

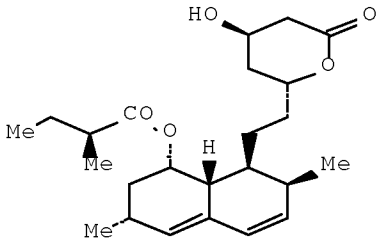


NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

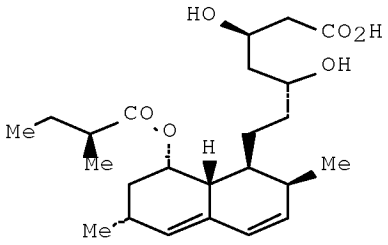
GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 29

STEREO ATTRIBUTES: NONE
L63 SCR 2127
L64 33 SEA FILE=REGISTRY SUB=L58 SSS FUL L61 NOT L63

```
L65        3561 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L64
L66           1 SEA FILE=REGISTRY ABB=ON  PLU=ON  "MEVINOLINIC ACID"/CN
L67             SEL  PLU=ON  L66 1- CHEM :      10 TERMS
L68         162 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L67
L69         164 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L68 OR MEVINOLINIC(W)ACID OR
                MEVINOLINATE
L70         119 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L65 AND L69
L74         328 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L65(L)(BMF OR PREP OR BPN)/RL

L75          30 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L70 AND L74


=> D IBIB ABS HITSTR L75 1-30

L75  ANSWER 1 OF 30  HCAPLUS  COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER:         2007:769874  HCAPLUS  Full-text
TITLE:                    Process for preparation and purification of lovastatin
INVENTOR(S):              Jaswinderjit, Singh; Bhavesh, Patel; Chetan, Patel
PATENT ASSIGNEE(S):       Alembic Limited, India
SOURCE:                   Indian Pat. Appl., 17pp.
                          CODEN: INXXBQ
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.           KIND   DATE        APPLICATION NO.         DATE
     ---------------      ----   --------    --------------------    --------
     IN 2005MU01389        A     20070629    IN 2005-MU1389          20051108
PRIORITY APPLN. INFO.:                       IN 2005-MU1389          20051108
GI
```



I



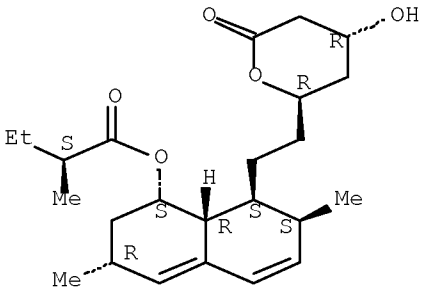
II

AB An improved process was disclosed for the preparation and purification of lovastatin (I), a therapeutically useful HMG-CoA reductase inhibitor. The process comprised treating a fermentation broth containing lovastatin acid (II) with a mineral acid, such as HCl, H2SO4, or H3PO4, to adjust the pH of the broth to 2-4, heating the acidified broth to 40-80°, for 18-25 h, and concentration and purification of the desired lactonization product I with a solution of a base, such as Na2CO3, followed by purification using filtration or centrifugation.

IT 75330-75-5P, Lovastatin
RL: BPN (Biosynthetic preparation); PUR (Purification or recovery); SPN (Synthetic preparation); THU (Therapeutic use); BIOL

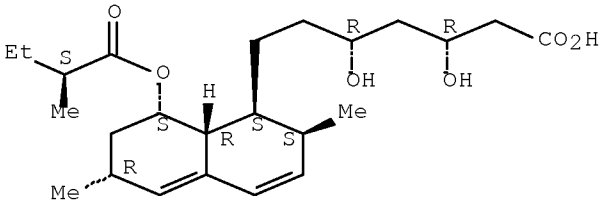
(Biological study); PREP (Preparation); USES (Uses)
(process for preparation via lactonization of in a fermentation broth containing
lovastatin open-chain acid and purification of lovastatin, a pharmaceutically useful cholesterol lowering agent)
RN 75330-75-5 HCAPLUS
CN Butanoic acid, 2-methyl-, (1S,3R,7S,8S,8aR)-1,2,3,7,8,8a-hexahydro-3,7-dimethyl-8-[2-[(2R,4R)-tetrahydro-4-hydroxy-6-oxo-2H-pyran-2-yl]ethyl]-1-naphthalenyl ester, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



IT 75225-51-3P, Lovastatin acid
RL: BPN (Biosynthetic preparation); RCT (Reactant); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(process for preparation via lactonization of in a fermentation broth containing
lovastatin open-chain acid and purification of lovastatin, a pharmaceutically useful cholesterol lowering agent)
RN 75225-51-3 HCAPLUS
CN 1-Naphthaleneheptanoic acid, 1,2,6,7,8,8a-hexahydro-β,δ-dihydroxy-2,6-dimethyl-8-[(2S)-2-methyl-1-oxobutoxy]-, (βR,δR,1S,2S,6R,8S,8aR)- (CA INDEX NAME)

Absolute stereochemistry.



L75 ANSWER 2 OF 30 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2007:756336 HCAPLUS Full-text
DOCUMENT NUMBER: 147:404891
TITLE: A macrokinetic modelling of the biosynthesis of lovastatin by Aspergillus terreus
AUTHOR(S): Bizukojc, Marcin; Ledakowicz, Stanislaw
CORPORATE SOURCE: Department of Bioprocess Engineering, Technical

University of Lodz, Lodz, 90-924, Pol.
SOURCE: Journal of Biotechnology (2007), 130(4), 422-435
CODEN: JBITD4; ISSN: 0168-1656
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

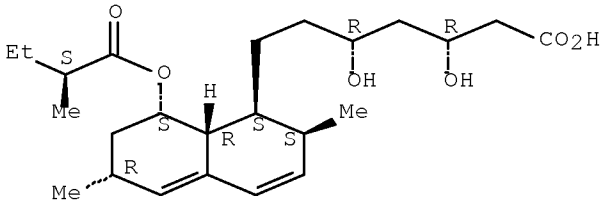
AB In this work a simple kinetic model to describe the biosynthesis of lovastatin by Aspergillus terreus ATCC 20542 was proposed. Several series of expts. were conducted at different media compns. The concns. of C- and N-sources were changed over a wide range and so were the initial biomass concns. From these runs the relationships ruling the substrates uptake, biomass and product formation were learnt. Lovastatin biosynthesis appeared to be partly growth associated The inhibitive effect of organic nitrogen on lovastatin biosynthesis was found and lactose appeared to be an important limiting substrate in the formation of lovastatin. The parameters of the model were evaluated on the basis of the kinetic data obtained in the sep. expts. made in triplicate at two chosen media compns. Other results obtained at different media compns. were independent of the ones mentioned above and used for the verification of the model. The validity of the model was also examined for the lactose-fed fed-batch run. Finally, a sensitivity anal. of the model parameters was performed. The formulated model, although relatively simplified, described the exptl. data quite well and could be regarded as the background for further attempts to math. describe the process of lovastatin biosynthesis.

IT 75225-51-3P, Mevinolinic acid
75330-75-5P, Lovastatin
RL: BMF (Bioindustrial manufacture); BIOL (Biological study); PREP (Preparation)
(macrokinetic modeling of biosynthesis of lovastatin by Aspergillus terreus)

RN 75225-51-3 HCAPLUS

CN 1-Naphthaleneheptanoic acid, 1,2,6,7,8,8a-hexahydro-β,δ-dihydroxy-2,6-dimethyl-8-[(2S)-2-methyl-1-oxobutoxy]-, (βR,δR,1S,2S,6R,8S,8aR)- (CA INDEX NAME)

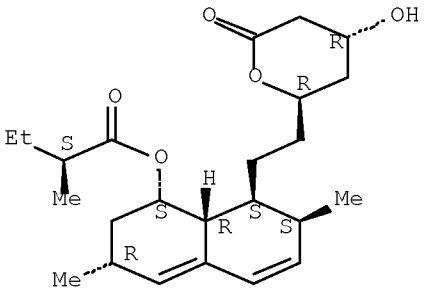
Absolute stereochemistry.



RN 75330-75-5 HCAPLUS

CN Butanoic acid, 2-methyl-, (1S,3R,7S,8S,8aR)-1,2,3,7,8,8a-hexahydro-3,7-dimethyl-8-[2-[(2R,4R)-tetrahydro-4-hydroxy-6-oxo-2H-pyran-2-yl]ethyl]-1-naphthalenyl ester, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

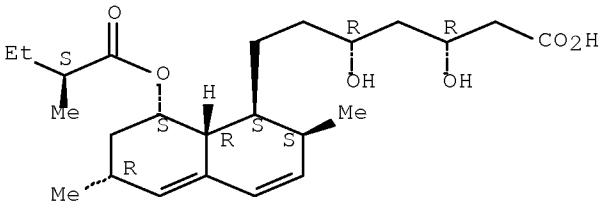
L75 ANSWER 3 OF 30 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:871125 HCAPLUS Full-text
DOCUMENT NUMBER: 145:270234
TITLE: A fermentor for solid-state fermentation and in-situ extraction of the products
INVENTOR(S): Narayan, Shri Kumar Surya; Majumdar, Kiran
PATENT ASSIGNEE(S): Biocon India Limited, India
SOURCE: Indian, 42 pp.
CODEN: INXXAP
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
IN 191600	A1	20031206	IN 2001-CA548	20010925
PRIORITY APPLN. INFO.:			IN 2001-CA548	20010925

AB The present invention discloses a process for production and extraction of various fermentation products by solid-state fermentation and a fermentor that is amenable for cultivation of microorganisms and extraction of the products. Detailed schematics and descriptions of this vessel are presented. Also presented are several examples of the use of the fermentor in the production and extraction of a variety of microbial products.

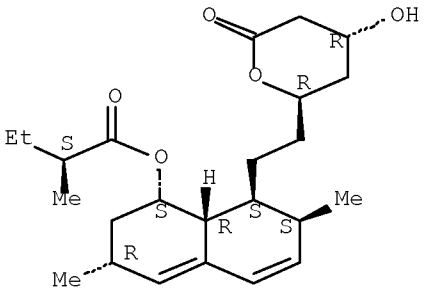
IT 75225-51-3P, Mevinolinic acid
RL: BMF (Bioindustrial manufacture); CPS (Chemical process); PEP (Physical, engineering or chemical process); PUR (Purification or recovery); RCT (Reactant); BIOL (Biological study); PREP (Preparation); PROC (Process); RACT (Reactant or reagent)
(fermentor for solid-state fermentation and in-situ extraction of products)
RN 75225-51-3 HCAPLUS
CN 1-Naphthaleneheptanoic acid, 1,2,6,7,8,8a-hexahydro-β,δ-dihydroxy-2,6-dimethyl-8-[(2S)-2-methyl-1-oxobutoxy]-, (βR,δR,1S,2S,6R,8S,8aR)- (CA INDEX NAME)

Absolute stereochemistry.



IT 75330-75-5P, Lovastatin
RL: IMF (Industrial manufacture); PUR (Purification or recovery); PREP (Preparation)
(fermentor for solid-state fermentation and in-situ extraction of products)
RN 75330-75-5 HCAPLUS
CN Butanoic acid, 2-methyl-, (1S,3R,7S,8S,8aR)-1,2,3,7,8,8a-hexahydro-3,7-dimethyl-8-[2-[(2R,4R)-tetrahydro-4-hydroxy-6-oxo-2H-pyran-2-yl]ethyl]-1-naphthalenyl ester, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



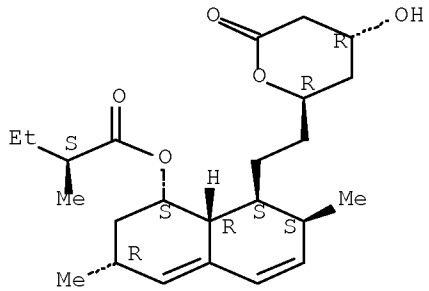
L75 ANSWER 4 OF 30 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:308254 HCAPLUS Full-text
DOCUMENT NUMBER: 145:209323
TITLE: Effect of substrate composition on the biosynthesis of lovastatin by Aspergillus terreus
AUTHOR(S): Bizukojc, Marcin; Ledakowicz, Stanislaw
CORPORATE SOURCE: Katedra Inz. Bioprocesowej, Politech. Lodzka, Lodz, Pol.
SOURCE: Inzynieria i Aparatura Chemiczna (2005), 44(4S), 9-10
CODEN: IZACAX; ISSN: 0368-0827
PUBLISHER: SIMPRESS
DOCUMENT TYPE: Journal
LANGUAGE: Polish
AB The influence of type and concentration of sources of carbon (glucose, lactose) and nitrogen (glutamic acid, casein hydrolyzate, yeast extract) in culture media on biosynthesis of mevinolinic acid (lovastatin) by Aspergillus terreus strain ATCC20542 was examined The use of lactose as C source led to better yields of mevinolinic acid than the use of glucose during .apprx.7-day culture. A pos. effect of N deficiency of the mevinolinic acid biosynthesis yield was seen. The type of N source was of high significance as with some N components (casein hydrolyzate) an inhibition of biosynthesis of mevinolinic

acid was observed The combination of lactose with yeast extract was most effective.

IT 75330-75-5P, Lovastatin
RL: BPN (Biosynthetic preparation); BIOL (Biological study); PREP (Preparation)
(culture medium carbon and nitrogen sources effects on yields of lovastatin biosynthesis by Aspergillus terreus ATCC20542)

RN 75330-75-5 HCAPLUS
CN Butanoic acid, 2-methyl-, (1S,3R,7S,8S,8aR)-1,2,3,7,8,8a-hexahydro-3,7-dimethyl-8-[2-[(2R,4R)-tetrahydro-4-hydroxy-6-oxo-2H-pyran-2-yl]ethyl]-1-naphthalenyl ester, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



L75 ANSWER 5 OF 30 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:1305392 HCAPLUS Full-text
DOCUMENT NUMBER: 145:187115
TITLE: The influence of environmental factors on mycelial growth and biosynthesis of lovastatin by Aspergillus terreus
AUTHOR(S): Bizukojc, Marcin; Ledakowicz, Stanislaw
CORPORATE SOURCE: Katedra Inz. Bioprocesowej, Politech. Lodzka, Lodz, 93-005, Pol.
SOURCE: Biotechnologia (2005), (Monogr. 2), 25-36
CODEN: BIECEV; ISSN: 0860-7796
PUBLISHER: Instytut Chemii Bioorganicznej PAN
DOCUMENT TYPE: Journal
LANGUAGE: Polish

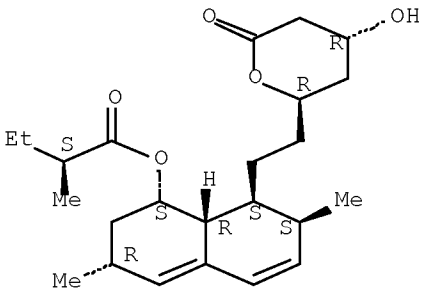
AB The influence of environmental factors on mycelial biomass growth and mevinolinic acid (lovastatin) production by Aspergillus terreus strain ATCC-20542 was studied. The optimum culture medium nutrient sources of carbon (glycerol, lactose, glucose) and nitrogen (casein peptone, yeast extract, Na glutamate) medium, influence of B vitamin supplementation, and influence N source on biomass elemental composition, mycelial growth and pellet formation kinetics were examined The best mevinolinic acid yield was obtained with N-deficient medium (C/N ratio >100) supplemented with B vitamins, lactose, and yeast extract as C and N sources.

IT 75330-75-5P, Lovastatin
RL: BPN (Biosynthetic preparation); BIOL (Biological study); PREP (Preparation)
(environmental factors effects on Aspergillus terreus mycelial growth and biosynthesis of lovastatin)

RN 75330-75-5 HCAPLUS
CN Butanoic acid, 2-methyl-, (1S,3R,7S,8S,8aR)-1,2,3,7,8,8a-hexahydro-3,7-

dimethyl-8-[2-[(2R,4R)-tetrahydro-4-hydroxy-6-oxo-2H-pyran-2-yl]ethyl]-1-naphthalenyl ester, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



L75 ANSWER 6 OF 30 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:1086245 HCAPLUS Full-text
DOCUMENT NUMBER: 143:365736
TITLE: Fungus strain Aspergillus terreus 44-62 as producer of lovastatin, industrial method for isolation of lovastatin and method for lactonization of statins
INVENTOR(S): Dzhavakhiya, V. G.; Voinova, T. M.; Vavilova, N. A.; Santsevich, N. I.; Vinokurova, N. G.; Kadomtseva, V. M.; Dzhavakhiya, V. V.; Mishin, A. G.
PATENT ASSIGNEE(S): Buyanovskii, Eduard Konstantinovich, Russia
SOURCE: Russ., 13 pp.
CODEN: RUXXE7
DOCUMENT TYPE: Patent
LANGUAGE: Russian
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
RU 2261901	C2	20051010	RU 2003-130693	20031017

PRIORITY APPLN. INFO.: RU 2003-130693 20031017

AB A new highly productive strain of A. terreus 44-62 producing lovastatin is presented; other usable fungi are A. oryzae and A. obscurus. The method for lovastatin isolation and for lactonization of statins, such as lovastatin and simvastatin, is described. The lovastatin isolation involves extraction of medium with fungus biomass, extract concentration under vacuum, lovastatin lactonization in the absence of solvent and presence of desiccating agents (MgSO4, NaSO4, CaCl2, silica gel, Sephadex, mol. sieves, etc.) at 60-80°C, washing with organic solvents (benzene, toluene, solvent mixts.), clarification with alumina or activated charcoal, and crystallization of the final product from ethanol or water. The biomass extraction with organic solvents uses Et acetate or Bu acetate and biomass medium is adjusted to pH 2-5 by adding HCl, H3PO4, H2SO4 or NH4OH. The lactonization process yields statins in crystalline form directly and practically without dimmer and acid impurities. The invention allows highly profitable manufacturing of lovastatin at high yields (>70%), low cost, and quality parameters corresponding to Pharmacopoeia requirements.

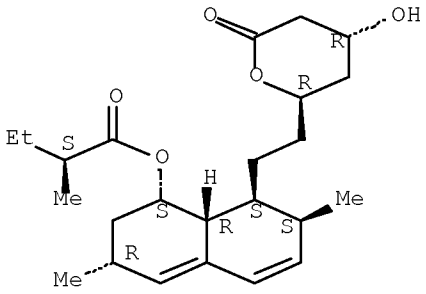
IT 75330-75-5P, Lovastatin

RL: BPN (Biosynthetic preparation); PUR (Purification or recovery); BIOL (Biological study); PREP (Preparation)
(Aspergillus terreus fungus strain 44-62 as producer of lovastatin, industrial method for lovastatin isolation and method for lactonization of statin drugs)

RN 75330-75-5 HCAPLUS

CN Butanoic acid, 2-methyl-, (1S,3R,7S,8S,8aR)-1,2,3,7,8,8a-hexahydro-3,7-dimethyl-8-[2-[(2R,4R)-tetrahydro-4-hydroxy-6-oxo-2H-pyran-2-yl]ethyl]-1-naphthalenyl ester, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



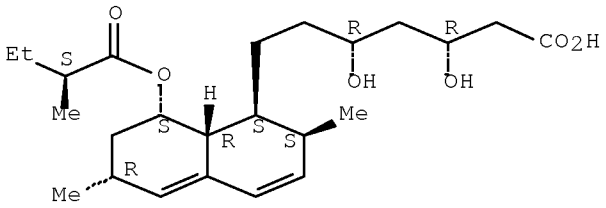
IT 75225-51-3P, Lovastatin acid

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(Aspergillus terreus fungus strain 44-62 as producer of lovastatin, industrial method for lovastatin isolation and method for lactonization of statin drugs)

RN 75225-51-3 HCAPLUS

CN 1-Naphthaleneheptanoic acid, 1,2,6,7,8,8a-hexahydro-β,δ-dihydroxy-2,6-dimethyl-8-[(2S)-2-methyl-1-oxobutoxy]-, (βR,δR,1S,2S,6R,8S,8aR)- (CA INDEX NAME)

Absolute stereochemistry.



L75 ANSWER 7 OF 30 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2005:347000 HCAPLUS Full-text

DOCUMENT NUMBER: 142:391044

TITLE: Production and purification of lovastatin

INVENTOR(S): Vaishnav, Sanjay Kumar; Thakur, Bhupendra Harishchandra; Kadam, Subhash Rajaram

PATENT ASSIGNEE(S): Lupin Limited, India

SOURCE: PCT Int. Appl., 29 pp.

CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005035515	A1	20050421	WO 2003-IN333	20031014
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2540068	A1	20031014	CA 2003-2540068	20031014
AU 2003290396	A1	20050427	AU 2003-290396	20031014
EP 1673361	A1	20060628	EP 2003-782759	20031014
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, SK				
IN 2006MN00221	A	20070608	IN 2006-MN221	20060224
US 2007238885	A1	20071011	US 2006-571192	20061220
PRIORITY APPLN. INFO.:			WO 2003-IN333 W	20031014

OTHER SOURCE(S): CASREACT 142:391044

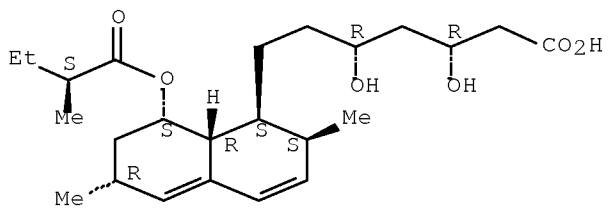
AB A method for the manufacture of lovastatin of formula is disclosed. The method comprises of: lactonization of mevinolinic acid and isolation of impure lovastatin, purification of impure lovastatin, and optionally, repurifn. of pure lovastatin from a mixture of alumina and a water miscible solvent.

IT 75225-51-3P, Mevinolinic acid
RL: BMF (Bioindustrial manufacture); CPS (Chemical process); PEP (Physical, engineering or chemical process); PUR (Purification or recovery); RCT (Reactant); BIOL (Biological study); PREP (Preparation); PROC (Process); RACT (Reactant or reagent)
(production and purification of lovastatin)

RN 75225-51-3 HCAPLUS

CN 1-Naphthaleneheptanoic acid, 1,2,6,7,8,8a-hexahydro-β,δ-dihydroxy-2,6-dimethyl-8-[(2S)-2-methyl-1-oxobutoxy]-, (βR,δR,1S,2S,6R,8S,8aR)- (CA INDEX NAME)

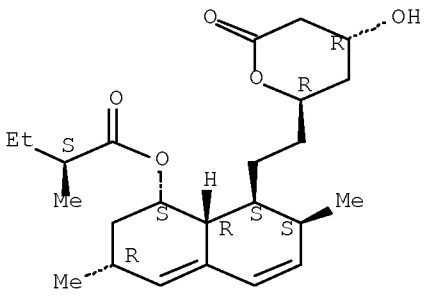
Absolute stereochemistry.



IT 75330-75-5P, Lovastatin
RL: IMF (Industrial manufacture); PUR (Purification or recovery);

PREP (Preparation)
(production and purification of lovastatin)
RN 75330-75-5 HCAPLUS
CN Butanoic acid, 2-methyl-, (1S,3R,7S,8S,8aR)-1,2,3,7,8,8a-hexahydro-3,7-dimethyl-8-[2-[(2R,4R)-tetrahydro-4-hydroxy-6-oxo-2H-pyran-2-yl]ethyl]-1-naphthalenyl ester, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

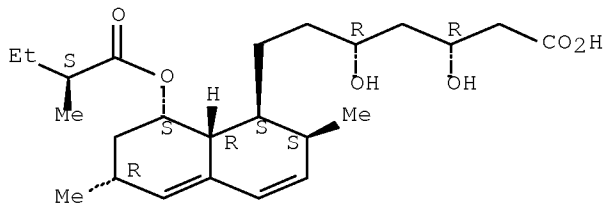
L75 ANSWER 8 OF 30 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:218552 HCAPLUS Full-text
DOCUMENT NUMBER: 142:480843
TITLE: Enhanced lovastatin production by solid state fermentation of Monascus ruber
AUTHOR(S): Xu, Bao-Jun; Wang, Qi-Jun; Jia, Xiao-Qin; Sung, Chang-Keun
CORPORATE SOURCE: Department of Food Science and Technology, College of Agriculture and Biotechnology, Chungnam National University, Taejon, 305-764, S. Korea
SOURCE: Biotechnology and Bioprocess Engineering (2005), 10(1), 78-84
CODEN: BBEIAU; ISSN: 1226-8372
PUBLISHER: Korean Society for Biotechnology and Bioengineering
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The purpose of this study was to optimize the solid state cultivation of Monascus ruber on sterile rice. A single-level-multiple-factor and a single-factor-multiple-level exptl. design were employed to determine the optimal medium constituents and to optimize carbon and nitrogen source concns. for lovastatin production Simultaneous quant. analyses of the β-hydroxyacid form and β-hydroxylactone for of lovastatin were performed by the high performance liquid chromatog. (HPLC) method with a UV photodiode-array (PDA) detector. The total lovastatin yield (4.apprx.6 mg/g, average of five repeats) was achieved by adding soybean powder, glycerol, sodium nitrate, and acetic acid at optimized levels after 14 days of fermentation The maximal yield of lovastatin under the optimal composition of the medium increased by almost 2 times the yield observed prior to optimization. The exptl. results also indicated that the β-hydroxylactone form of lovastatin (LFL) and the β-hydroxyacid form of lovastatin (AFL) simultaneously existed in solid state cultures of Monascus ruber, while the latter was the dominant form in the middle-late stage of continued fermentation These results indicate that

optimized culture conditions can be used for industrial production of lovastatin to obtain high yields.

IT 75225-51-3P, Lovastatin acid
75330-75-5P, Lovastatin
RL: BMF (Bioindustrial manufacture); BIOL (Biological study); PREP (Preparation)
(enhanced lovastatin production by solid state fermentation of Monascus ruber)

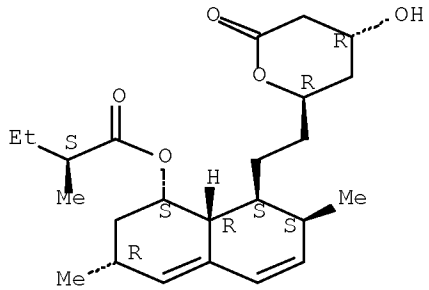
RN 75225-51-3 HCAPLUS
CN 1-Naphthaleneheptanoic acid, 1,2,6,7,8,8a-hexahydro-β,δ-dihydroxy-2,6-dimethyl-8-[(2S)-2-methyl-1-oxobutoxy]-, (βR,δR,1S,2S,6R,8S,8aR)- (CA INDEX NAME)

Absolute stereochemistry.



RN 75330-75-5 HCAPLUS
CN Butanoic acid, 2-methyl-, (1S,3R,7S,8S,8aR)-1,2,3,7,8,8a-hexahydro-3,7-dimethyl-8-[2-[(2R,4R)-tetrahydro-4-hydroxy-6-oxo-2H-pyran-2-yl]ethyl]-1-naphthalenyl ester, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L75 ANSWER 9 OF 30 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:120911 HCAPLUS Full-text
DOCUMENT NUMBER: 142:197756
TITLE: Lactonization process for the production of statin lactones
INVENTOR(S): Chandrapa, Ravindra; Poornaprajna, Achraya; Ganesh, Sambasivam
PATENT ASSIGNEE(S): Biocon Limited, India
SOURCE: PCT Int. Appl., 15 pp.

CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005012279	A1	20050210	WO 2003-IN264	20030804
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2003263579	A1	20050215	AU 2003-263579	20030804

PRIORITY APPLN. INFO.: WO 2003-IN264 A 20030804
OTHER SOURCE(S): CASREACT 142:197756; MARPAT 142:197756
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

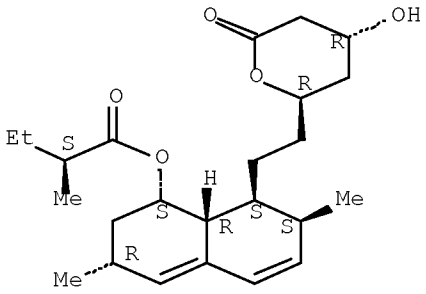
AB A process for preparation of lactone statins I [G = (un)substituted alkyl, aryl, heteroaryl] comprises reacting a statin acid or salt II [X = H, metal, amine] with sulfuric acid, where the sulfuric acid is added in one portion, at less than 0.8 equiv of the statin salt or acid, at less than -15° for <1 h in a water-miscible solvent (e.g., acetonitrile). Thus, simvastatin (III) was prepared from simvastatin ammonium salt (IV·+NH4) in MeCN containing butylated hydroxanisole to which H2SO4 was added.

IT 75330-75-5P, Lovastatin
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(lactonization process for the production of statin lactones)

RN 75330-75-5 HCAPLUS

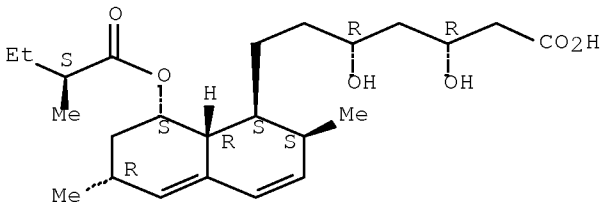
CN Butanoic acid, 2-methyl-, (1S,3R,7S,8S,8aR)-1,2,3,7,8,8a-hexahydro-3,7-dimethyl-8-[2-[(2R,4R)-tetrahydro-4-hydroxy-6-oxo-2H-pyran-2-yl]ethyl]-1-naphthalenyl ester, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



IT 75225-51-3, Lovastatin acid
RL: RCT (Reactant); RACT (Reactant or reagent)
(lactonization process for the production of statin lactones)
RN 75225-51-3 HCAPLUS
CN 1-Naphthaleneheptanoic acid, 1,2,6,7,8,8a-hexahydro-β,δ-dihydroxy-2,6-dimethyl-8-[(2S)-2-methyl-1-oxobutoxy]-, (βR,δR,1S,2S,6R,8S,8aR)- (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L75 ANSWER 10 OF 30 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:1039250 HCAPLUS Full-text
DOCUMENT NUMBER: 141:409886
TITLE: Improved process for the preparation of lovastatin
INVENTOR(S): Vaid, Sudhir; Maurya, Rajkumar; Sharma, Sunita; Upadhyay, G. C.
PATENT ASSIGNEE(S): Ranbaxy Laboratories Ltd., India
SOURCE: Indian, 14 pp.
CODEN: INXXAP
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
IN 186317	A1	20010804	IN 1997-DE1064	19970425

PRIORITY APPLN. INFO.: IN 1997-DE1064 19970425
OTHER SOURCE(S): CASREACT 141:409886
AB An improved process for the preparation of lovastatin is claimed, which process comprises fermentation of microfungus of genus Aspergillus in

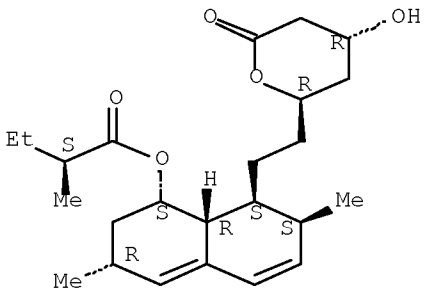
conventional culture media, adding assimilable C source continuously or in calculated batches during fermentation to maintain the pH of the fermentation broth at 5.5-7.5 and to maintain the residual sugar level in the fermentation broth at 0.1-2.8%. The fermentation broth is acidified, mixed with extraction solvent, and refluxed at 60° to obtain mevinolinic acid. The mevinolinic acid or its salt thus obtained is then subjected to the lactonization reaction, wherein the mevinolinic acid or its salt is bound to a solid support such as resin, as herein described and eluting to convert the mevinolinic acid or its salt to lovastatin.

IT 75330-75-5P, Lovastatin
RL: BMF (Bioindustrial manufacture); BPN (Biosynthetic preparation); PUR (Purification or recovery); BIOL (Biological study); PREP (Preparation)
(process for the preparation of lovastatin)

RN 75330-75-5 HCAPLUS

CN Butanoic acid, 2-methyl-, (1S,3R,7S,8S,8aR)-1,2,3,7,8,8a-hexahydro-3,7-dimethyl-8-[2-[(2R,4R)-tetrahydro-4-hydroxy-6-oxo-2H-pyran-2-yl]ethyl]-1-naphthalenyl ester, (2S)- (CA INDEX NAME)

Absolute stereochemistry.

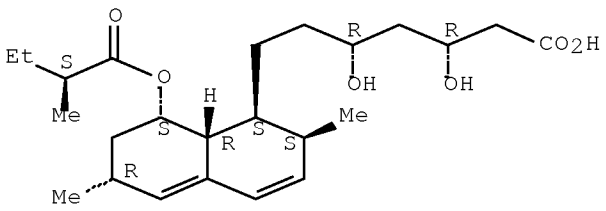


IT 75225-51-3P, Mevinolinic acid
RL: BPN (Biosynthetic preparation); RCT (Reactant); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(process for the preparation of lovastatin)

RN 75225-51-3 HCAPLUS

CN 1-Naphthaleneheptanoic acid, 1,2,6,7,8,8a-hexahydro-β,δ-dihydroxy-2,6-dimethyl-8-[(2S)-2-methyl-1-oxobutoxy]-, (βR,δR,1S,2S,6R,8S,8aR)- (CA INDEX NAME)

Absolute stereochemistry.



L75 ANSWER 11 OF 30 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2004:924792 HCAPLUS Full-text
DOCUMENT NUMBER: 141:378918
TITLE: Process for the isolation and purification of mevinolin from fermentation broth
INVENTOR(S): Keri, Vilmos; Hoegye, Irma; Jekkel, Antonia; Bagdi, Ilona; Ambrus, Gabor; Jakab, Attila; Andor, Attila; Deak, Lajos; Szabo, Istvan; Balint, Janos; Scheidl, Zsuzsanna; Deli, Etelka; Horvath, Gyula; Szabo, Csaba; Lang, Ildiko; Szekely, Imre; Moravcsik, Imre; Kovacs, Vera; Matyas, Szabolcs; Sztaray, Zsuzsanna; Eszenyi, Laszlo; Ilkoey, Eva
PATENT ASSIGNEE(S): Hung.
SOURCE: U.S., 5 pp., Cont.-in-part of U.S. Ser. No. 659,961, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6812007	B1	20041102	US 2000-578587	20000419
HU 210867	B	19951030	HU 1992-3458	19921104
WO 9410328	A1	19940511	WO 1993-HU51	19930908
W: AT, CA, DE, ES, US				
US 2006223150	A1	20061005	US 2004-842221	20040510

PRIORITY APPLN. INFO.:

HU 1992-3458	A	19921104
WO 1993-HU51	B2	19930908
US 1994-269150	B1	19940630
US 1996-659961	B2	19960607
US 2000-578587	A1	20000419

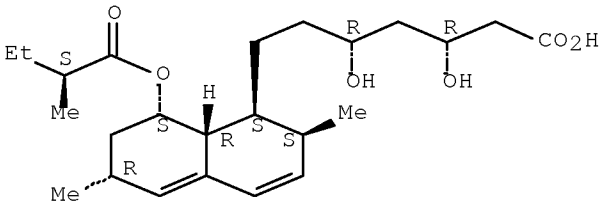
AB In a process for preparing mevinolin by fermentation of a biomass in a fermentation liquor, which includes dissolving mevinolin from the biomass into the fermentation liquor, and separating the biomass from the fermentation liquor to obtain a separated fermentation liquor, separating the mevinolin from the separated fermentation liquor, and recovering the end product, the improvement which comprises carrying out the dissolving at a pH between 7.5 and about 10, and the separating of the mevinolin is carried out at a pH between about 4.5 and about 1.

IT 75225-51-3P 75330-75-5P, Mevinolin
RL: BMF (Bioindustrial manufacture); PUR (Purification or recovery); BIOL (Biological study); PREP (Preparation)
(process for isolation and purification of mevinolin from fermentation broth)

RN 75225-51-3 HCAPLUS

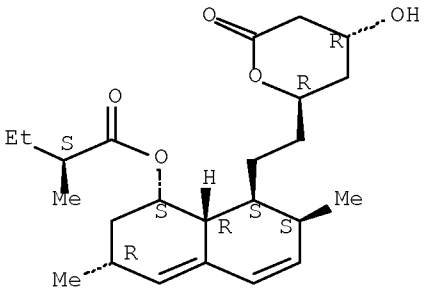
CN 1-Naphthaleneheptanoic acid, 1,2,6,7,8,8a-hexahydro-β,δ-dihydroxy-2,6-dimethyl-8-[(2S)-2-methyl-1-oxobutoxy]-, (βR,δR,1S,2S,6R,8S,8aR)- (CA INDEX NAME)

Absolute stereochemistry.



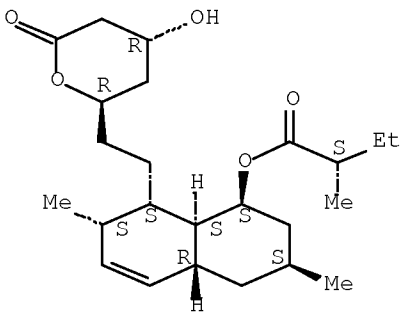
RN 75330-75-5 HCAPLUS
CN Butanoic acid, 2-methyl-, (1S,3R,7S,8S,8aR)-1,2,3,7,8,8a-hexahydro-3,7-dimethyl-8-[2-[(2R,4R)-tetrahydro-4-hydroxy-6-oxo-2H-pyran-2-yl]ethyl]-1-naphthalenyl ester, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



IT 77517-29-4P, DihydroMevinolin
RL: BYP (Byproduct); PREP (Preparation)
(process for isolation and purification of mevinolin from fermentation broth)
RN 77517-29-4 HCAPLUS
CN Butanoic acid, 2-methyl-, (1S,3S,4aR,7S,8S,8aS)-1,2,3,4,4a,7,8,8a-octahydro-3,7-dimethyl-8-[2-[(2R,4R)-tetrahydro-4-hydroxy-6-oxo-2H-pyran-2-yl]ethyl]-1-naphthalenyl ester, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

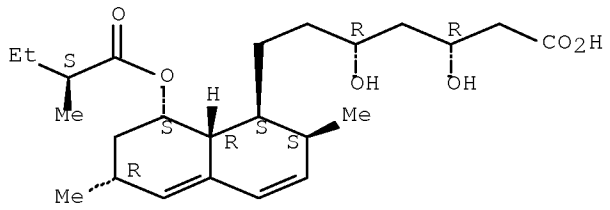
L75 ANSWER 12 OF 30 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:879830 HCAPLUS Full-text
DOCUMENT NUMBER: 141:313031
TITLE: A process for the lactonization and purification of antihypercholesterolemic agents
INVENTOR(S): Venkates, Needamangalam Srinivasa; Ganesh, Sambasivam
PATENT ASSIGNEE(S): Helix Biotech Limited, India
SOURCE: Indian, 17 pp.
CODEN: INXXAP
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
IN 184325	A1	20000805	IN 1996-MA2203	19961206
PRIORITY APPLN. INFO.:			IN 1996-MA2203	19961206

AB A process for the purification of the lactone form of antihypercholesterolemic agents of the , such as lovastatin, mevastatin diol and the like from the corresponding acid or salt forms such as mevinolinic acid, triol acid and mevinic acid.

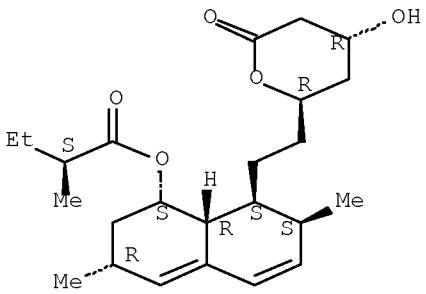
IT 75225-51-3DP, Mevinolinic acid, acid or salt forms
RL: BMF (Bioindustrial manufacture); CPS (Chemical process); PEP (Physical, engineering or chemical process); RCT (Reactant); BIOL (Biological study); PREP (Preparation); PROC (Process); RACT (Reactant or reagent)
(process for lactonization and purification of antihypercholesterolemic agents)
RN 75225-51-3 HCAPLUS
CN 1-Naphthaleneheptanoic acid, 1,2,6,7,8,8a-hexahydro-β,δ-dihydroxy-2,6-dimethyl-8-[(2S)-2-methyl-1-oxobutoxy]-, (βR,δR,1S,2S,6R,8S,8aR)- (CA INDEX NAME)

Absolute stereochemistry.



IT 75330-75-5P, Lovastatin
RL: IMF (Industrial manufacture); PREP (Preparation)
(process for lactonization and purification of antihypercholesterolemic agents)
RN 75330-75-5 HCAPLUS
CN Butanoic acid, 2-methyl-, (1S,3R,7S,8S,8aR)-1,2,3,7,8,8a-hexahydro-3,7-dimethyl-8-[2-[(2R,4R)-tetrahydro-4-hydroxy-6-oxo-2H-pyran-2-yl]ethyl]-1-naphthalenyl ester, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



L75 ANSWER 13 OF 30 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:445740 HCAPLUS Full-text
DOCUMENT NUMBER: 140:405572
TITLE: Process for the recovery and purification of lovastatin from fermentation broth
INVENTOR(S): Patel, Dinesh; Bhattacharya, Parimal Kumar
PATENT ASSIGNEE(S): Themis Chemical Ltd., India
SOURCE: Indian, 10 pp.
CODEN: INXXAP
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
IN 181829	A1	19981003	IN 1996-BO446	19960829

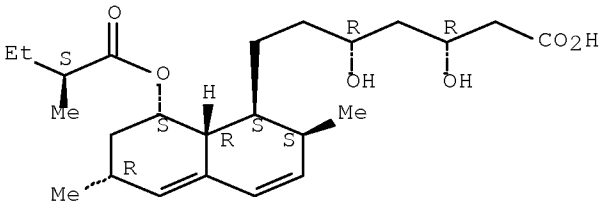
PRIORITY APPLN. INFO.: IN 1996-BO446 19960829

AB A process for recovery of lovastatin of desired purity from fermentation broth by precipitation of alkaline lovastatin acid followed by extraction and lactonization.

IT 75225-51-3P, Lovastatin acid
RL: BMF (Bioindustrial manufacture); CPS (Chemical process); PEP (Physical, engineering or chemical process); PUR (Purification or recovery); RCT (Reactant); BIOL (Biological study); PREP (Preparation); PROC (Process); RACT (Reactant or reagent)
(process for recovery and purification of lovastatin from fermentation broth)

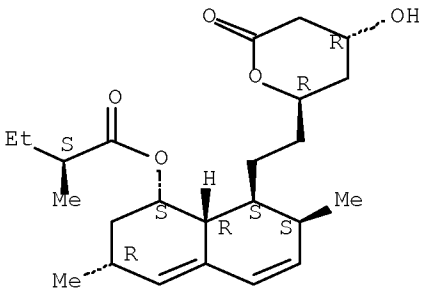
RN 75225-51-3 HCAPLUS
CN 1-Naphthaleneheptanoic acid, 1,2,6,7,8,8a-hexahydro-β,δ-dihydroxy-2,6-dimethyl-8-[(2S)-2-methyl-1-oxobutoxy]-, (βR,δR,1S,2S,6R,8S,8aR)- (CA INDEX NAME)

Absolute stereochemistry.



IT 75330-75-5P, LOVASTATIN
RL: IMF (Industrial manufacture); PUR (Purification or recovery); PREP (Preparation)
(process for recovery and purification of lovastatin from fermentation broth)
RN 75330-75-5 HCAPLUS
CN Butanoic acid, 2-methyl-, (1S,3R,7S,8S,8aR)-1,2,3,7,8,8a-hexahydro-3,7-dimethyl-8-[2-[(2R,4R)-tetrahydro-4-hydroxy-6-oxo-2H-pyran-2-yl]ethyl]-1-naphthalenyl ester, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



L75 ANSWER 14 OF 30 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:445739 HCAPLUS Full-text
DOCUMENT NUMBER: 140:405571
TITLE: Recovery of lovastatin from the fermentation broth by counter current extraction
INVENTOR(S): Patel, Dinesh; Bhattacharya, Parimal Kumar
PATENT ASSIGNEE(S): Themis Chemical Ltd., India
SOURCE: Indian, 11 pp.
CODEN: INXXAP
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
IN 181828	A1	19981003	IN 1996-BO445	19960829

PRIORITY APPLN. INFO.: IN 1996-BO445 19960829

AB A process for the recovery of lovastatin of desired purity from the fermentation broth by counter current extraction comprises the following steps: fermentation broth containing lovastatin acid is treated with acids

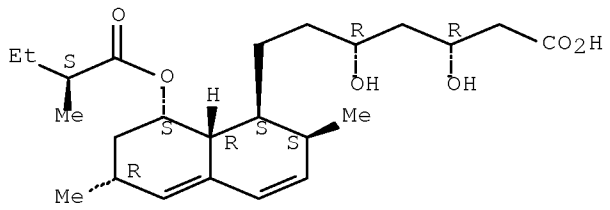
like sulfuric acid, hydrochloric acid or phosphoric acids. The treated broth is extracted with solvents like Et acetate, Bu acetate using counter-current extraction The aqueous phase containing mycelium is discarded and the organic phase containing alkaline lovastatin acid form along with other organic impurities is collected. The organic phase is partly concentrated and then treated with water containing acid and subsequently with alkali to remove the organic impurities. The purified organic phase is refluxed and concentrated in the presence of acids like sulfuric acid to obtain complete lactonization. The concentrated solution is given repeated charcoal treatment and then cooled to give crude lovastatin. The crude lovastatin obtained is crystallized using methanol or ethanol as solvent to obtain lovastatin of desired purity.

IT 75225-51-3P, Lovastatin acid
RL: BMF (Bioindustrial manufacture); CPS (Chemical process); PEP (Physical, engineering or chemical process); PUR (Purification or recovery); RCT (Reactant); BIOL (Biological study); PREP (Preparation); PROC (Process); RACT (Reactant or reagent)
(recovery of lovastatin from fermentation broth by counter current extraction)

RN 75225-51-3 HCAPLUS

CN 1-Naphthaleneheptanoic acid, 1,2,6,7,8,8a-hexahydro-β,δ-dihydroxy-2,6-dimethyl-8-[(2S)-2-methyl-1-oxobutoxy]-, (βR,δR,1S,2S,6R,8S,8aR)- (CA INDEX NAME)

Absolute stereochemistry.

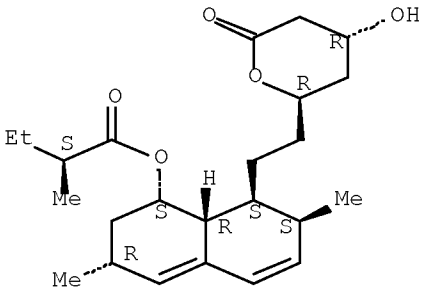


IT 75330-75-5P, LOVASTATIN
RL: IMF (Industrial manufacture); PUR (Purification or recovery); PREP (Preparation)
(recovery of lovastatin from fermentation broth by counter current extraction)

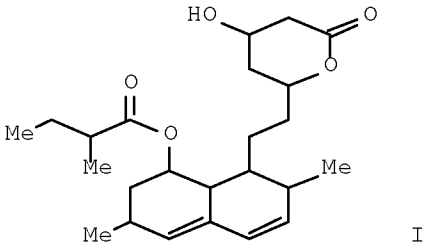
RN 75330-75-5 HCAPLUS

CN Butanoic acid, 2-methyl-, (1S,3R,7S,8S,8aR)-1,2,3,7,8,8a-hexahydro-3,7-dimethyl-8-[2-[(2R,4R)-tetrahydro-4-hydroxy-6-oxo-2H-pyran-2-yl]ethyl]-1-naphthalenyl ester, (2S)- (CA INDEX NAME)

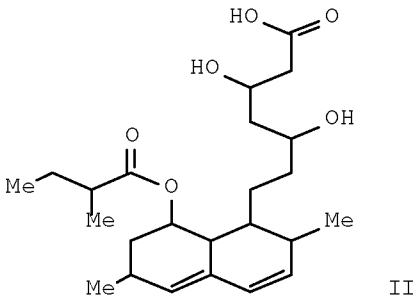
Absolute stereochemistry.



L75 ANSWER 15 OF 30 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:533081 HCAPLUS Full-text
DOCUMENT NUMBER: 140:4102
TITLE: Screening of lovastatin production by filamentous fungi
AUTHOR(S): Samiee, Siamak M.; Moazami, Nasrin; Haghighi, Saeid; Mohseni, Farzaneh Aziz; Mirdamadi, Saeid; Bakhtiari, Mohammad Reza
CORPORATE SOURCE: Dept. of Biotechnology, Pasteur Institute of Iran, Iranian Research Organization for Science and Technology, Tehran, Iran
SOURCE: Iranian Biomedical Journal (2003), 7(1), 29-33
CODEN: IBJRAN; ISSN: 1028-852X
PUBLISHER: Pasteur Institute of Iran
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I



II

AB In the present study, 110 fungal strains of Persian Type Culture Collection (PTCC), including some selected strains isolated in various screening projects, were tested for their potentiality to produce lovastatin, a competitive inhibitor of 3-hydroxy-3-methylglutaryl-CoA reductase (HMG-CoA reductase), the rate-limiting enzyme of cholesterol biosynthesis. The fungal strains were cultivated in a two-stage submerged fermentation followed by screening by TLC. All pos. results were evaluated by confirmatory HPLC. Nine species of four genera were found to be lovastatin producers and the fermentation broth exts. contained both the open hydroxy acid and the lactone forms of lovastatin (I and II, resp.). Aspergillus terreus was the best

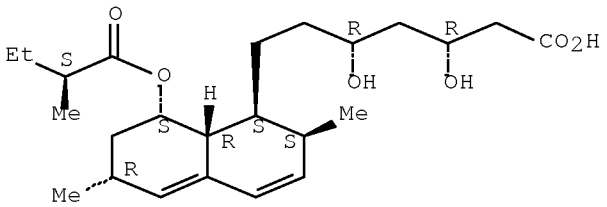
lovastatin producing strain with a level of 55 mg lovastatin per L of screening production medium.

IT 75225-51-3P, Lovastatin acid
75330-75-5P, Lovastatin lactone
RL: BMF (Bioindustrial manufacture); BPN (Biosynthetic preparation); BIOL (Biological study); PREP (Preparation)
(screening of lovastatin production by filamentous fungi)

RN 75225-51-3 HCAPLUS

CN 1-Naphthaleneheptanoic acid, 1,2,6,7,8,8a-hexahydro-β,δ-dihydroxy-2,6-dimethyl-8-[(2S)-2-methyl-1-oxobutoxy]-, (βR,δR,1S,2S,6R,8S,8aR)- (CA INDEX NAME)

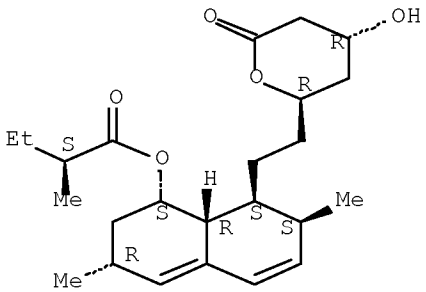
Absolute stereochemistry.



RN 75330-75-5 HCAPLUS

CN Butanoic acid, 2-methyl-, (1S,3R,7S,8S,8aR)-1,2,3,7,8,8a-hexahydro-3,7-dimethyl-8-[2-[(2R,4R)-tetrahydro-4-hydroxy-6-oxo-2H-pyran-2-yl]ethyl]-1-naphthalenyl ester, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L75 ANSWER 16 OF 30 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2002:607035 HCAPLUS Full-text

DOCUMENT NUMBER: 138:292509

TITLE: Concentration of lovastatin, mevinolinic acid and other sterol biosynthesis inhibitors produced by Penicillium citrinum 89 on Diapak C 16 cartridges

AUTHOR(S): Baranova, N. A.; Kreier, V. G.; Egorov, N. S.

CORPORATE SOURCE: M.V. Lomonosov Moscow State University, Russia

SOURCE: Antibiotiki i Khimioterapiya (2002), 47(4), 3-6
CODEN: ANKHEW; ISSN: 0235-2990

PUBLISHER: Izdatel'skii Dom "Krasnaya Ploshchad"
DOCUMENT TYPE: Journal
LANGUAGE: Russian

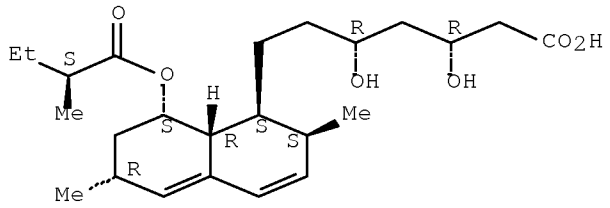
AB The method of lovastatin and mevinolinic acid known as competitive inhibitors of HMG-CoA-reductase and produced by micromycetes was elaborated. The inhibitors from diluted water solns. were fully sorbed on Diapak C 16 cartridges. The rate of inhibitors elution from the cartridges was more than 95%. The cartridges may be used for concentrating lovastatin group inhibitors from the culture media. The inhibitor synthesis by the P. citrinum 89 was investigated with the use of Diapak C 16 cartridges. The UV spectrum of inhibitor produced by P. citrinum 89 was identical with compactin spectrum and had absorbance maximum at 230, 237 and 247 nm.

IT 75225-51-3P, Mevinolinic acid
75330-75-5P, Lovastatin
RL: BPN (Biosynthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(concentration of lovastatin, mevinolinic acid and other sterol biosynthesis inhibitors produced by Penicillium citrinum 89 on Diapak C 16 cartridges)

RN 75225-51-3 HCAPLUS

CN 1-Naphthaleneheptanoic acid, 1,2,6,7,8,8a-hexahydro-β,δ-dihydroxy-2,6-dimethyl-8-[(2S)-2-methyl-1-oxobutoxy]-, (βR,δR,1S,2S,6R,8S,8aR)- (CA INDEX NAME)

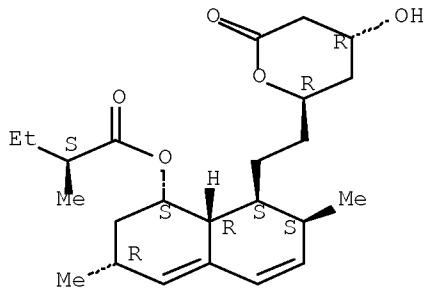
Absolute stereochemistry.



RN 75330-75-5 HCAPLUS

CN Butanoic acid, 2-methyl-, (1S,3R,7S,8S,8aR)-1,2,3,7,8,8a-hexahydro-3,7-dimethyl-8-[2-[(2R,4R)-tetrahydro-4-hydroxy-6-oxo-2H-pyran-2-yl]ethyl]-1-naphthalenyl ester, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



L75 ANSWER 17 OF 30 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:10435 HCAPLUS Full-text
DOCUMENT NUMBER: 136:84764
TITLE: Process for the isolation of lovastatin
INVENTOR(S): Kumar, Parveen; Raman, S.; Narula, Pardeep
PATENT ASSIGNEE(S): Ranbaxy Laboratories Limited, India
SOURCE: PCT Int. Appl., 14 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002000615	A2	20020103	WO 2001-IB1087	20010620
WO 2002000615	A3	20020530		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
IN 192861	A1	20040522	IN 2000-DE630	20000630
CA 2412566	A1	20020103	CA 2001-2412566	20010620
AU 200164173	A	20020108	AU 2001-64173	20010620
EP 1299340	A2	20030409	EP 2001-938499	20010620
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
HU 2003001423	A2	20030828	HU 2003-1423	20010620
BR 2001012024	A	20030909	BR 2001-12024	20010620
ZA 2003000006	A	20031027	ZA 2003-6	20030102
US 2003215932	A1	20031120	US 2003-311944	20030424
US 7052886	B2	20060530		

PRIORITY APPLN. INFO.: IN 2000-DE630 A 20000630
WO 2001-IB1087 W 20010620

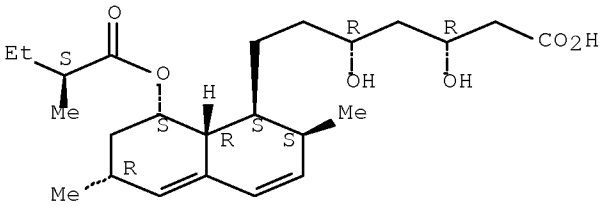
AB The process for the preparation and isolation of the hypolipemic active substance lovastatin in substantially pure form having a purity of at least 95% which comprises lactonizing the mevinolinic acid to lovastatin in a totally aqueous medium.

IT 75225-51-3P, Mevinolinic acid
RL: BMF (Bioindustrial manufacture); RCT (Reactant); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(process for isolation of lovastatin)

RN 75225-51-3 HCAPLUS

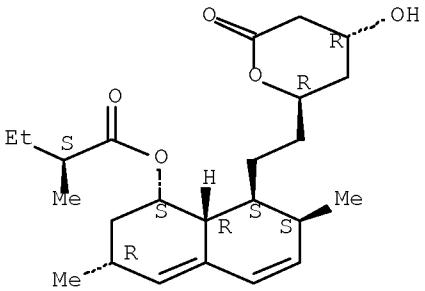
CN 1-Naphthaleneheptanoic acid, 1,2,6,7,8,8a-hexahydro-β,δ-dihydroxy-2,6-dimethyl-8-[(2S)-2-methyl-1-oxobutoxy]-, (βR,δR,1S,2S,6R,8S,8aR)- (CA INDEX NAME)

Absolute stereochemistry.



IT 75330-75-5P, Lovastatin
RL: IMF (Industrial manufacture); PUR (Purification or recovery); PREP (Preparation)
(process for isolation of lovastatin)
RN 75330-75-5 HCAPLUS
CN Butanoic acid, 2-methyl-, (1S,3R,7S,8S,8aR)-1,2,3,7,8,8a-hexahydro-3,7-dimethyl-8-[2-[(2R,4R)-tetrahydro-4-hydroxy-6-oxo-2H-pyran-2-yl]ethyl]-1-naphthalenyl ester, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



L75 ANSWER 18 OF 30 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2000:249543 HCAPLUS Full-text
DOCUMENT NUMBER: 132:278495
TITLE: Monascus koji rich in monacolin K, its manufacture, and products using the koji
INVENTOR(S): Kadoya, Takumi; Tanabe, Nobukazu
PATENT ASSIGNEE(S): Gunze, Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 4 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2000106835	A	20000418	JP 1998-315295	19980930
PRIORITY APPLN. INFO.:			JP 1998-315295	19980930

AB In manufacture of koji rich in hypocholesteremic monacolin K (I), bran is added to koji materials, water content is maintained at 30-45%, and a temperature in a late stage of the koji-making process is kept at ≤27° for ≥3 days. Also claimed are the Monascus koji and products manufactured using the

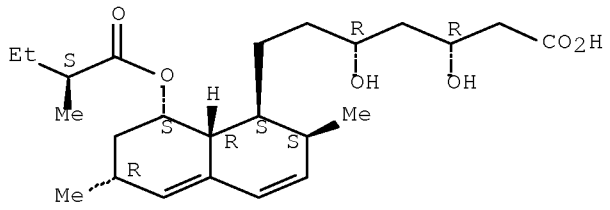
koji. Monascus pilosus IFO 4520 was cultured in a mixture of water-soaked water-soaked polished rice and 7% (based on the rice) wheat bran at 30° for the first 4 days and at 25° for 4 days while keeping H2O content 36-41% to give 101 mg I/100 g dry weight, vs. 32 mg/100 g dry weight for a control koji using no wheat bran.

IT 75225-51-3P 75330-75-5P, Monacolin K lactone
RL: BMF (Bioindustrial manufacture); BPN (Biosynthetic preparation); FFD (Food or feed use); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(manufacture of Monascus koji rich in monacolin K using bran as additives under control of water content and temperature)

RN 75225-51-3 HCAPLUS

CN 1-Naphthaleneheptanoic acid, 1,2,6,7,8,8a-hexahydro-β,δ-dihydroxy-2,6-dimethyl-8-[(2S)-2-methyl-1-oxobutoxy]-, (βR,δR,1S,2S,6R,8S,8aR)- (CA INDEX NAME)

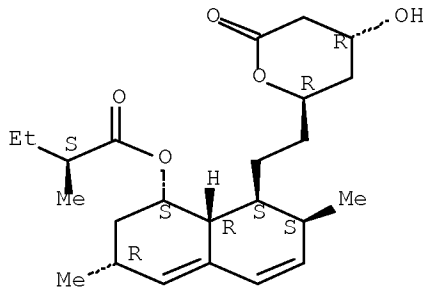
Absolute stereochemistry.



RN 75330-75-5 HCAPLUS

CN Butanoic acid, 2-methyl-, (1S,3R,7S,8S,8aR)-1,2,3,7,8,8a-hexahydro-3,7-dimethyl-8-[2-[(2R,4R)-tetrahydro-4-hydroxy-6-oxo-2H-pyran-2-yl]ethyl]-1-naphthalenyl ester, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



L75 ANSWER 19 OF 30 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2000:247254 HCAPLUS Full-text
DOCUMENT NUMBER: 132:278494
TITLE: Monascus koji rich in monacolin K and glucosamine manufactured from bran and products using the koji
INVENTOR(S): Kadoya, Takumi; Tanabe, Nobukazu
PATENT ASSIGNEE(S): Gunze, Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 3 pp.

CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2000106834	A	20000418	JP 1998-315294	19980930

PRIORITY APPLN. INFO.: JP 1998-315294 19980930

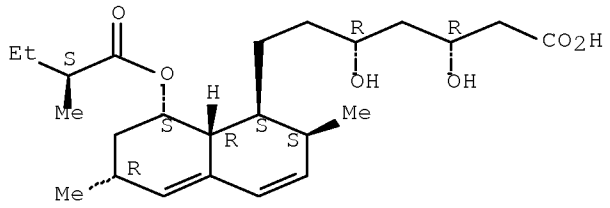
AB Koji, which preferably contains total monacolin K (I, acid and lactone forms) at ≥100 mg/100 g dry weight and glucosamine (II) at ≥5 mg/g dry weight, is manufactured from bran and Monascus. Also claimed are products manufactured from the koji. The koji shows antihypertensive effect based on II, and I has hypocholesteremic effect. Rice germs were steamed and inoculated with Monascus pilosus IFO 4520. The koji material was aerobically cultured at 30° for 4 days and at 25° for 4 days to give 11.3 mg II/g dry weight and 241 mg I/100 g dry weight, vs. 3.6 mg/g dry weight and 28 mg/100 g dry weight, resp., for a control koji using polished rice.

IT 75225-51-3P 75330-75-5P, Monacolin K lactone
RL: BMF (Bioindustrial manufacture); BPN (Biosynthetic preparation); FFD (Food or feed use); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(monacolin K and glucosamine high-producing koji from bran and Monascus with antihypertensive and hypocholesteremic effects)

RN 75225-51-3 HCAPLUS

CN 1-Naphthaleneheptanoic acid, 1,2,6,7,8,8a-hexahydro-β,δ-dihydroxy-2,6-dimethyl-8-[(2S)-2-methyl-1-oxobutoxy]-, (βR,δR,1S,2S,6R,8S,8aR)- (CA INDEX NAME)

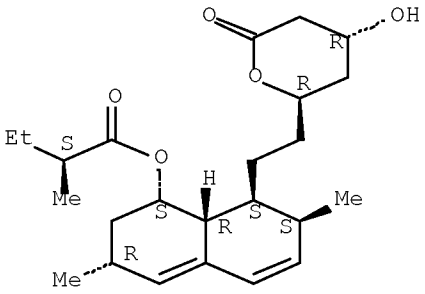
Absolute stereochemistry.



RN 75330-75-5 HCAPLUS

CN Butanoic acid, 2-methyl-, (1S,3R,7S,8S,8aR)-1,2,3,7,8,8a-hexahydro-3,7-dimethyl-8-[2-[(2R,4R)-tetrahydro-4-hydroxy-6-oxo-2H-pyran-2-yl]ethyl]-1-naphthalenyl ester, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



L75 ANSWER 20 OF 30 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2000:210141 HCAPLUS Full-text
DOCUMENT NUMBER: 132:241979
TITLE: Process for obtaining HMG-CoA reductase inhibitors of high purity
INVENTOR(S): Grahek, Rok; Milivojevic, Dusan; Bastarda, Andrej
PATENT ASSIGNEE(S): Lek Pharmaceutical and Chemical Company D.D., Slovenia
SOURCE: PCT Int. Appl., 25 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000017182	A1	20000330	WO 1999-IB1553	19990917
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
SI 20072	A	20000430	SI 1998-241	19980918
CA 2343645	A1	20000330	CA 1999-2343645	19990917
AU 9955284	A	20000410	AU 1999-55284	19990917
AU 766630	B2	20031023		
EP 1114040	A1	20010711	EP 1999-941797	19990917
EP 1114040	B1	20041208		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
HU 2001002997	A2	20011228	HU 2001-2997	19990917
JP 2002526486	T	20020820	JP 2000-574092	19990917
JP 3795755	B2	20060712		
NZ 509582	A	20031031	NZ 1999-509582	19990917
RU 2235098	C2	20040827	RU 2001-108381	19990917
AT 284396	T	20041215	AT 1999-941797	19990917
RO 121116	B1	20061229	RO 2001-289	19990917
SK 285868	B6	20071004	SK 2000-2002	19990917
US 6695969	B1	20040224	US 2001-720952	20010103
HR 2001000045	A1	20011231	HR 2001-45	20010116
HR 2001000045	B1	20050831		

BG 105348	A	20011130	BG 2001-105348		20010316
BG 64676	B1	20051130			
US 2004138294	A1	20040715	US 2003-698009		20031030
US 7141602	B2	20061128			
IN 2004DN03747	A	20050401	IN 2004-DN3747		20041125
US 2007032549	A1	20070208	US 2006-581637		20061016
PRIORITY APPLN. INFO.:			SI 1998-241	A	19980918
			WO 1999-IB1553	W	19990917
			US 2001-720952	A2	20010103
			US 2003-698009	A3	20031030

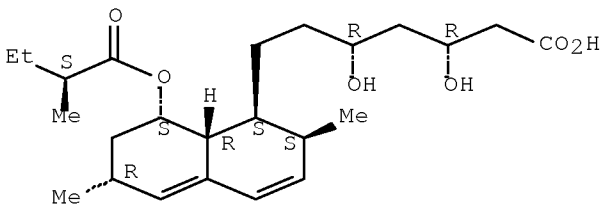
AB Lovastatin, pravastatin, simvastatin, mevastatin, atorvastatin, and derivs. and analogs are known as HMG-CoA reductase inhibitors and are used as antihypercholesterolemic agents. The majority of them are produced by fermentation using microorganisms of different species identified as species belonging to Aspergillus, Monascus, Nocardia, Amycolatopsis, Mucor or Penicillium genus, some are obtained by treating the fermentation products using the method of chemical synthesis or they are the products of total chemical synthesis. The purity of the active ingredient is an important factor for manufacturing the safe and effective pharmaceutical, especially if the pharmaceutical product must be taken on a longer term basis in the treatment or prevention of high plasma cholesterol. The accumulation of the impurities from the pharmaceuticals of lower purity may cause many side effects during the medical treatment. The present invention relates to a new industrial process for the isolation of HMG-CoA reductase inhibitors using so-called displacement chromatog. Use of the invention enables to obtain HMG-CoA reductase inhibitors of high purity, with high yields, lower production costs and suitable ecol. balance. Crude sodium salt of pravastatin (HPLC purity 88%) was dissolved in the mobile phase A (distilled water), pH was adjusted to 7 with 0.2M aqueous NaOH solution and filtered. The column was equilibrated with mobile phase A. The sample obtained in the above manner was fed onto the Grom-Sil 120-ODS HE column (particle size 30 11 μm, column size 250 x 10 mm). The column was washed with the mobile phase B containing 7% of diethylene glycol monobutyl ether in mobile phase A at the flow rate of 4.5 mL/min. Absorbance was measured at 260 nm, and the 0.5 mL fractions were collected with an initial increase in the absorbance. When the signal decreased the column was washed with 25 mL of 70% MeOH. The fractions obtained were analyzed by the HPLC method. The fractions with a purity 99.5% were pooled. In the pooled fractions (7 mL), the HPLC purity was 99.8%.

IT 75225-51-3P 75330-75-5P, Lovastatin
RL: PUR (Purification or recovery); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(process for obtaining HMG-CoA reductase inhibitors of high purity)

RN 75225-51-3 HCAPLUS

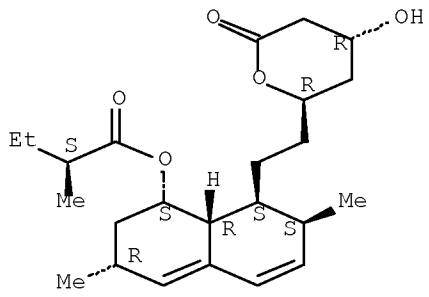
CN 1-Naphthaleneheptanoic acid, 1,2,6,7,8,8a-hexahydro-β,δ-dihydroxy-2,6-dimethyl-8-[(2S)-2-methyl-1-oxobutoxy]-, (βR,δR,1S,2S,6R,8S,8aR)- (CA INDEX NAME)

Absolute stereochemistry.



RN 75330-75-5 HCAPLUS
CN Butanoic acid, 2-methyl-, (1S,3R,7S,8S,8aR)-1,2,3,7,8,8a-hexahydro-3,7-dimethyl-8-[2-[(2R,4R)-tetrahydro-4-hydroxy-6-oxo-2H-pyran-2-yl]ethyl]-1-naphthalenyl ester, (2S)- (CA INDEX NAME)

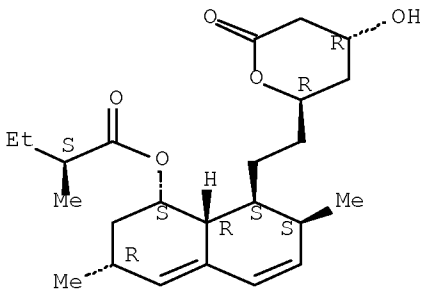
Absolute stereochemistry.



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

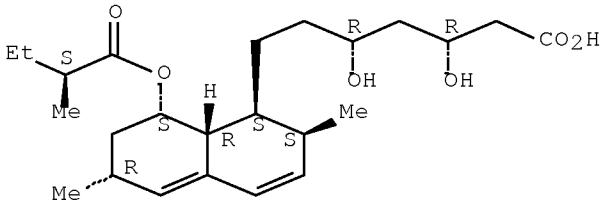
L75 ANSWER 21 OF 30 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1998:685701 HCAPLUS Full-text
DOCUMENT NUMBER: 130:65297
TITLE: Studies on the extraction and the lactonization of lovastatin in the process of isolation from the fermentation broth of Aspergillus terreus
AUTHOR(S): Lazarova, V.; Mindjova, K.; Georgieva, T.; Atanassova, T.
CORPORATE SOURCE: Chemical Pharmaceutical Research Inst., NIHFI Ltd., Sofia, 1756, Bulg.
SOURCE: Pharmazie (1998), 53(10), 727-728
CODEN: PHARAT; ISSN: 0031-7144
PUBLISHER: Govi-Verlag Pharmazeutischer Verlag
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The rate of isolation of lovastatin extracted from fermentation broth of Aspergillus terreus with CHCl3 and CH2Cl2 was 70 and 72%, with Et acetate and Bu acetate 62 and 65%. The quantity of lovastatin lactone exceeded that of lovastatin acid when extracted with halogenated hydrocarbons, i.e. lactonization occurred at room temperature A method for extraction, concentration, and crystallization (Et alc. or iso-Pr alc.) of lovastatin was described.
IT 75330-75-5P, Lovastatin
RL: BMF (Bioindustrial manufacture); BPR (Biological process); BSU (Biological study, unclassified); PUR (Purification or recovery); BIOL (Biological study); PREP (Preparation); PROC (Process)
(extraction and the lactonization of lovastatin in the process of isolation from the fermentation broth of Aspergillus terreus)
RN 75330-75-5 HCAPLUS
CN Butanoic acid, 2-methyl-, (1S,3R,7S,8S,8aR)-1,2,3,7,8,8a-hexahydro-3,7-dimethyl-8-[2-[(2R,4R)-tetrahydro-4-hydroxy-6-oxo-2H-pyran-2-yl]ethyl]-1-naphthalenyl ester, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



IT 75225-51-3, Lovastatin acid
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(extraction and the lactonization of lovastatin in the process of isolation from the fermentation broth of Aspergillus terreus)
RN 75225-51-3 HCAPLUS
CN 1-Naphthaleneheptanoic acid, 1,2,6,7,8,8a-hexahydro-β,δ-dihydroxy-2,6-dimethyl-8-[(2S)-2-methyl-1-oxobutoxy]-, (βR,δR,1S,2S,6R,8S,8aR)- (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L75 ANSWER 22 OF 30 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1997:205242 HCAPLUS Full-text
DOCUMENT NUMBER: 126:198639
TITLE: Process for the preparation of lovastatin
INVENTOR(S): Radez, Ivan; Benicki, Neda; Filipovic, Branislav; Zupancic, Silvia; Pokorny, Miroslav; Tihi, Jaroslav; Krasovec, Dusan; Zupancic, Martina
PATENT ASSIGNEE(S): Krka, Tovarna Zdravil, P.O., Slovenia
SOURCE: PCT Int. Appl., 34 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

WO 9705269		A1	19970213	WO 1996-SI16	19960716
W:	AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG				
RW:	KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA				
AU 9663263		A	19970226	AU 1996-63263	19960716
EP 842290		A1	19980520	EP 1996-922367	19960716
EP 842290		B1	20040128		
R:	DE				
JP 2000500642		T	20000125	JP 1997-507530	19960716
JP 3689429		B2	20050831		
HR 960357		B1	20041031	HR 1996-357	19960725
PRIORITY APPLN. INFO.:				SI 1995-238 A	19950727
				WO 1995-SI238 W	19950727
				WO 1996-SI16 W	19960716

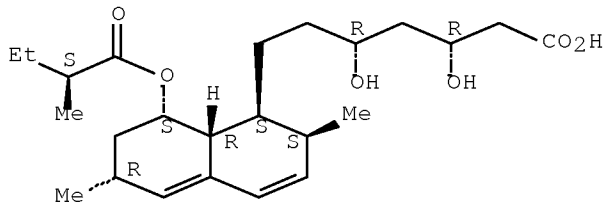
AB A process for preparing lovastatin is described which involves use of Aspergillus terreus var. aureus, which process results in very high yields of lovastatin even under conditions where conventionally used microorganisms are inhibited.

IT 75225-51-3P, Lovastatin acid
75330-75-5P, Lovastatin
RL: BMF (Bioindustrial manufacture); BPN (Biosynthetic preparation); BIOL (Biological study); PREP (Preparation)
(production of lovastatin by fermentation with Aspergillus terreus var. aureus)

RN 75225-51-3 HCAPLUS

CN 1-Naphthaleneheptanoic acid, 1,2,6,7,8,8a-hexahydro-β,δ-dihydroxy-2,6-dimethyl-8-[(2S)-2-methyl-1-oxobutoxy]-, (βR,δR,1S,2S,6R,8S,8aR)- (CA INDEX NAME)

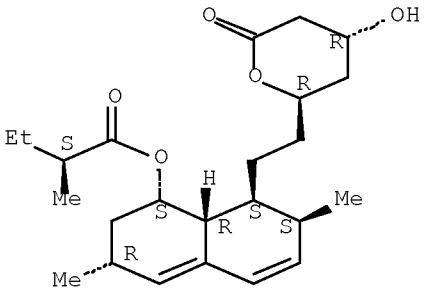
Absolute stereochemistry.



RN 75330-75-5 HCAPLUS

CN Butanoic acid, 2-methyl-, (1S,3R,7S,8S,8aR)-1,2,3,7,8,8a-hexahydro-3,7-dimethyl-8-[2-[(2R,4R)-tetrahydro-4-hydroxy-6-oxo-2H-pyran-2-yl]ethyl]-1-naphthalenyl ester, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



L75 ANSWER 23 OF 30 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1995:401300 HCAPLUS Full-text
DOCUMENT NUMBER: 122:158772
TITLE: Process for the isolation of lovastatin
INVENTOR(S): Hajko, Pavica; Vesel, Tanja; Radez, Ivan; Pokorny, Miroslav
PATENT ASSIGNEE(S): KRKR Trovarna Zdravil P.O., Slovenia
SOURCE: PCT Int. Appl., 15 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

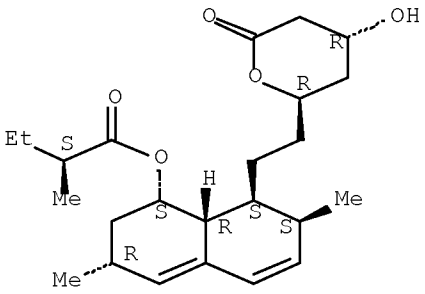
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9429292	A1	19941222	WO 1994-SI10	19940608
W: BG, BY, CA, CZ, FI, GE, HU, KG, LV, MD, NO, PL, RO, RU, SK, TJ, UA, US, UZ				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
CA 2164411	A1	19941222	CA 1994-2164411	19940608
CA 2164411	C	20020115		
EP 702679	A1	19960327	EP 1994-917872	19940608
EP 702679	B1	19980408		
R: AT, DE, ES, GB, IT, NL, PT				
HU 72836	A2	19960528	HU 1995-3385	19940608
HU 216647	B	19990728		
AT 164842	T	19980415	AT 1994-917872	19940608
CZ 283540	B6	19980415	CZ 1995-3251	19940608
RU 2114912	C1	19980710	RU 1996-101191	19940608
SK 280255	B6	19991008	SK 1995-1480	19940608
RO 115444	B1	20000228	RO 1995-2127	19940608
PL 178163	B1	20000331	PL 1994-311880	19940608
US 5712130	A	19980127	US 1995-591669	19951205
PRIORITY APPLN. INFO.:			SI 1993-303 A	19930608
			WO 1994-SI10 W	19940608

AB A process for the isolation of the hypolipemic active substance lovastatin from a fermentation broth, mycelium, or filtrate of Aspergillus terreus or Aspergillus oryzae by extraction with BuOAc is disclosed. Simultaneously with concentration of the extract, lactonization takes place. There follows a direct crystallization of lovastatin in the lactone form from BuOAc.

IT 75330-75-5P, Lovastatin
RL: BMF (Bioindustrial manufacture); BIOL (Biological study); PREP (Preparation)

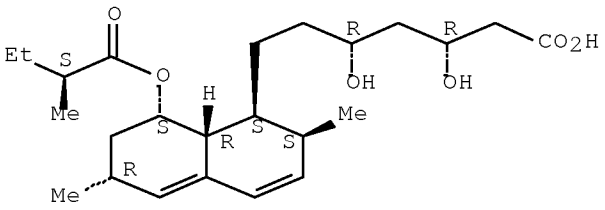
(isolation of lovastatin from a fermentation broth or Aspergillus by extraction,
lactonization, and crystallization in Bu acetate)
RN 75330-75-5 HCAPLUS
CN Butanoic acid, 2-methyl-, (1S,3R,7S,8S,8aR)-1,2,3,7,8,8a-hexahydro-3,7-dimethyl-8-[2-[(2R,4R)-tetrahydro-4-hydroxy-6-oxo-2H-pyran-2-yl]ethyl]-1-naphthalenyl ester, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



IT 75225-51-3P, Lovastatin acid
RL: BPN (Biosynthetic preparation); RCT (Reactant); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(isolation of lovastatin from a fermentation broth or Aspergillus by extraction,
lactonization, and crystallization in Bu acetate)
RN 75225-51-3 HCAPLUS
CN 1-Naphthaleneheptanoic acid, 1,2,6,7,8,8a-hexahydro-β,δ-dihydroxy-2,6-dimethyl-8-[(2S)-2-methyl-1-oxobutoxy]-, (βR,δR,1S,2S,6R,8S,8aR)- (CA INDEX NAME)

Absolute stereochemistry.



L75 ANSWER 24 OF 30 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1995:234836 HCAPLUS Full-text
DOCUMENT NUMBER: 122:8156
TITLE: Biotechnological production of lovastatin and/or mevinolinic acid
INVENTOR(S): Gunde-Cimerman, Nina; Friedrich, Jozica; Berovic, Marin; Cimerman, Aleksa; Benicki, Neda; Radez, Ivan; Pokorny, Miroslav
PATENT ASSIGNEE(S): KRKA, Tovarna Zdravil, p.o., Slovenia; Kemijski Institut

SOURCE: Ger. Offen., 4 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

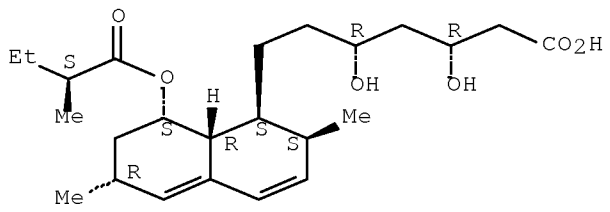
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 4402591	A1	19941020	DE 1994-4402591	19940128
PRIORITY APPLN. INFO.:			SI 1993-47 A	19930129

AB Lovastatin and/or mevinolinic acid are produced by surface or submerged cultivation of Pleurotus spp., e.g., P. ostreatus, P. sapidus, or P. saca. When the fermentation pH is adjusted to 3.0 at the completion of fermentation, the product is predominantly in the form of lovastatin, and when the pH is brought to 7.7, only mevinolinic acid is recovered. Both products are extracted from the broth and mycelium with MeOH.

IT 75225-51-3P, Mevinolinic acid
75330-75-5P, Lovastatin
RL: BMF (Bioindustrial manufacture); BIOL (Biological study); PREP (Preparation)
(biotechnol. production of lovastatin and/or mevinolinic acid)

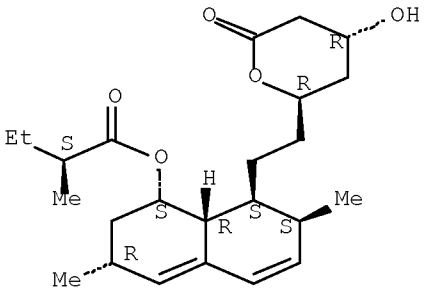
RN 75225-51-3 HCAPLUS
CN 1-Naphthaleneheptanoic acid, 1,2,6,7,8,8a-hexahydro-β,δ-dihydroxy-2,6-dimethyl-8-[(2S)-2-methyl-1-oxobutoxy]-, (βR,δR,1S,2S,6R,8S,8aR)- (CA INDEX NAME)

Absolute stereochemistry.



RN 75330-75-5 HCAPLUS
CN Butanoic acid, 2-methyl-, (1S,3R,7S,8S,8aR)-1,2,3,7,8,8a-hexahydro-3,7-dimethyl-8-[2-[(2R,4R)-tetrahydro-4-hydroxy-6-oxo-2H-pyran-2-yl]ethyl]-1-naphthalenyl ester, (2S)- (CA INDEX NAME)

Absolute stereochemistry.

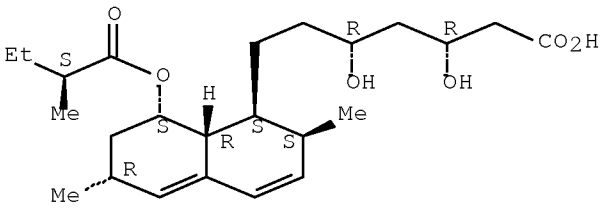


L75 ANSWER 25 OF 30 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1994:161756 HCAPLUS Full-text
DOCUMENT NUMBER: 120:161756
TITLE: Holotyp-strain Aspergillus obscurus for the manufacture of de mevinolin and/or β,5-dihydroxy-7-[1,2,6,7,8,8a-hexahydro-2,6-dimethyl-8-(2-methylbutyryloxy)naphthalen-1-yl]heptanoic acid.
INVENTOR(S): Jekkel Bokany, Antonia; Ilkoyl, Eva; Szabo, Istvan Mihaly; Ambrus, Gabor; Andor, Attila; Varga, Boesinger, Ilona; Moravcsik, Imre; Szabo, Istvan; Erdei, Jabis; et al.
PATENT ASSIGNEE(S): BIOGAL Gyogyszergyar, Hung.
SOURCE: Ger. Offen., 14 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 4320023	A1	19931223	DE 1993-4320023	19930617
CA 2098698	A1	19931218	CA 1993-2098698	19930617
CA 2098698	C	19980519		
ES 2064282	A1	19950116	ES 1993-1350	19930617
ES 2064282	B1	19950801		
US 5403728	A	19950404	US 1993-77364	19930617
AT 399722	B	19950725	AT 1993-1189	19930617
IN 176656	A1	19960817	IN 1993-MA418	19930617
PRIORITY APPLN. INFO.:			HU 1992-2020 A	19920617

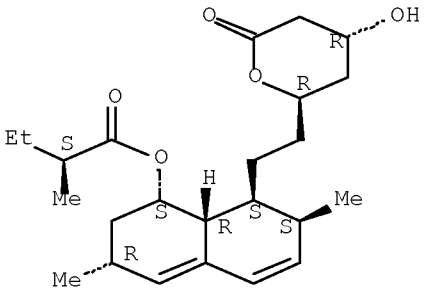
AB An imperfect holotype MV-1 A. obscurus strain was isolated, which is suitable for the manufacture of title compds. by submerged aerobic fermentation
IT 75225-51-3P 75330-75-5P, Mevinolin
RL: BMF (Bioindustrial manufacture); BIOL (Biological study); PREP (Preparation)
(manufacture of, by Aspergillus obscurus fermentation)
RN 75225-51-3 HCAPLUS
CN 1-Naphthaleneheptanoic acid, 1,2,6,7,8,8a-hexahydro-β,δ-dihydroxy-2,6-dimethyl-8-[(2S)-2-methyl-1-oxobutoxy]-, (βR,δR,1S,2S,6R,8S,8aR)- (CA INDEX NAME)

Absolute stereochemistry.



RN 75330-75-5 HCAPLUS
CN Butanoic acid, 2-methyl-, (1S,3R,7S,8S,8aR)-1,2,3,7,8,8a-hexahydro-3,7-dimethyl-8-[2-[(2R,4R)-tetrahydro-4-hydroxy-6-oxo-2H-pyran-2-yl]ethyl]-1-naphthalenyl ester, (2S)- (CA INDEX NAME)

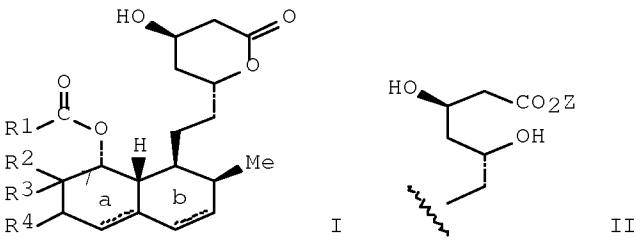
Absolute stereochemistry.



L75 ANSWER 26 OF 30 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1991:607855 HCAPLUS Full-text
DOCUMENT NUMBER: 115:207855
TITLE: Preparation of 7-substituted lovastatin derivatives as HMG-CoA reductase inhibitors
INVENTOR(S): Duggan, Mark E.; Halczenko, Wasyl; Hartman, George D.
PATENT ASSIGNEE(S): Merck and Co., Inc., USA
SOURCE: Eur. Pat. Appl., 40 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
EP 415488	A2	19910306	EP 1990-202270		19900824
EP 415488	A3	19910911			
EP 415488	B1	19940420			
R: CH, DE, FR, GB, IT, LI, NL					
CA 2024248	A1	19910301	CA 1990-2024248		19900829
JP 03184940	A	19910812	JP 1990-232278		19900831
US 5098931	A	19920324	US 1990-587598		19900924
PRIORITY APPLN. INFO.:			US 1989-401361	A	19890831
OTHER SOURCE(S):	MARPAT 115:207855				

GI



AB The title lactones [I; R1 = (un)substituted C1-10 alkyl, C1-10 alkoxy, (un)substituted C3-8 cycloalkyl, (un)substituted Ph, amino, heterocyclyl, etc.; R2, R3 = H, HO, R5O; R4 = H, HO, (un)substituted C1-10 alkyl; CR5 = C5-6 carbocyclyl; R5 = R(O)R7R8, CONR7R8, etc.; R7, R8 = H, (Ph)C1-3 alkyl, (un)substituted Ph, naphthyl, or heterocyclyl; a, b = optional bonds] and their acid forms II; Z = H, (un)substituted C1-5 alkyl, 2,3-dihydroxypropyl], useful as antihypercholesterolemic agents for the treatment of arteriosclerosis, hyperlipidemia, familial hypercholesterolemia, etc., were prepared by multistep derivatization of lovastatin. Thus, 7(S)-[1-(S)-hydroxyethyl]-isomer of lovastatin derivative I (R1 = EtCMe2, R2 = R4 = H, R3 = MeCHOH, a = b = bond) in vitro had relative HMG-CoA inhibition potency of 350 (compactin = 100) vs. 124 for 7(S)-[1-(R)-hydroxyethyl]-isomer of the same derivative

IT 75225-51-3P

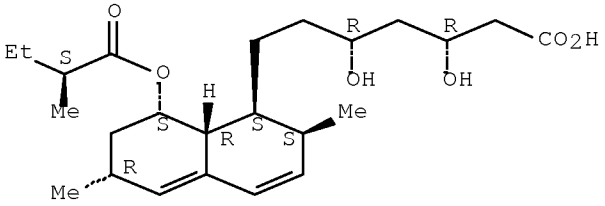
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation and reaction of, in preparation of HMG CoA reductase inhibitor)

RN 75225-51-3 HCAPLUS

CN 1-Naphthaleneheptanoic acid, 1,2,6,7,8,8a-hexahydro-β,δ-dihydroxy-2,6-dimethyl-8-[(2S)-2-methyl-1-oxobutoxy]-, (βR,δR,1S,2S,6R,8S,8aR)- (CA INDEX NAME)

Absolute stereochemistry.



IT 136432-22-9P 136432-23-0P 136432-24-1P 136432-25-2P 136451-32-6P

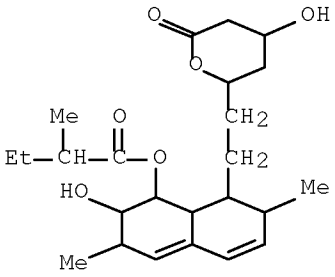
RL: SPN (Synthetic preparation); PREP (Preparation)

(preparation of, as HMG CoA reductase inhibitor)

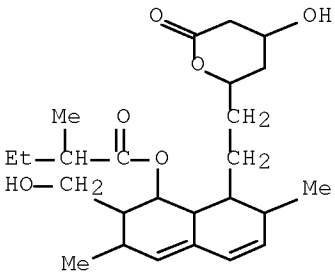
RN 136432-22-9 HCAPLUS

CN Butanoic acid, 2-methyl-, 1,2,3,7,8,8a-hexahydro-2-hydroxy-3,7-dimethyl-8-[2-(tetrahydro-4-hydroxy-6-oxo-2H-pyran-2-yl)ethyl]-1-naphthalenyl ester

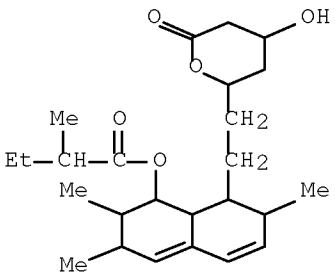
(CA INDEX NAME)



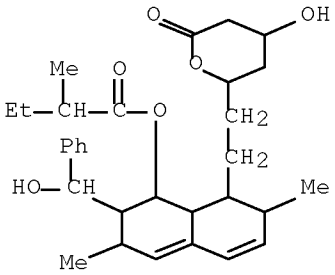
RN 136432-23-0 HCAPLUS
CN Butanoic acid, 2-methyl-, 1,2,3,7,8,8a-hexahydro-2-(hydroxymethyl)-3,7-dimethyl-8-[2-(tetrahydro-4-hydroxy-6-oxo-2H-pyran-2-yl)ethyl]-1-naphthalenyl ester (CA INDEX NAME)



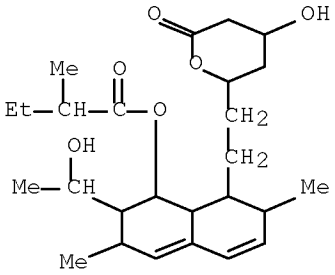
RN 136432-24-1 HCAPLUS
CN Butanoic acid, 2-methyl-, 1,2,3,7,8,8a-hexahydro-2,3,7-trimethyl-8-[2-(tetrahydro-4-hydroxy-6-oxo-2H-pyran-2-yl)ethyl]-1-naphthalenyl ester (CA INDEX NAME)



RN 136432-25-2 HCAPLUS
CN Butanoic acid, 2-methyl-, 1,2,3,7,8,8a-hexahydro-2-(hydroxyphenylmethyl)-3,7-dimethyl-8-[2-(tetrahydro-4-hydroxy-6-oxo-2H-pyran-2-yl)ethyl]-1-naphthalenyl ester (CA INDEX NAME)

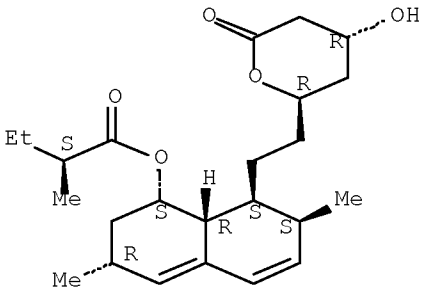


RN 136451-32-6 HCAPLUS
CN Butanoic acid, 2-methyl-, 1,2,3,7,8,8a-hexahydro-2-(1-hydroxyethyl)-3,7-dimethyl-8-[2-(tetrahydro-4-hydroxy-6-oxo-2H-pyran-2-yl)ethyl]-1-naphthalenyl ester (CA INDEX NAME)



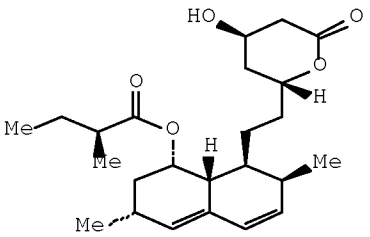
IT 75330-75-5, Lovastatin
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, in preparation of HMG CoA reductase inhibitor)
RN 75330-75-5 HCAPLUS
CN Butanoic acid, 2-methyl-, (1S,3R,7S,8S,8aR)-1,2,3,7,8,8a-hexahydro-3,7-dimethyl-8-[2-[(2R,4R)-tetrahydro-4-hydroxy-6-oxo-2H-pyran-2-yl]ethyl]-1-naphthalenyl ester, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



L75 ANSWER 27 OF 30 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1989:224922 HCAPLUS Full-text
DOCUMENT NUMBER: 110:224922
TITLE: The physiological disposition of lovastatin
AUTHOR(S): Duggan, D. E.; Chen, I. W.; Bayne, W. F.; Halpin, R. A.; Duncan, C. A.; Schwartz, M. S.; Stubbs, R. J.; Vickers, S.
CORPORATE SOURCE: Merck Inst. Ther. Res., Merck Sharp and Dohme Research Lab., West Point, PA, 19486, USA
SOURCE: Drug Metabolism and Disposition (1989), 17(2), 166-73
CODEN: DMDSAI; ISSN: 0090-9556
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I

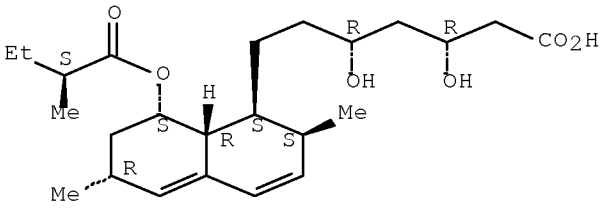
AB Lovastatin (I) is a prodrug lactone whose open chain β-hydroxy-acid (HA) is a potent inhibitor of hydroxymethylglutaryl-CoA-reductase and thus of cholesterol synthesis. Because the liver is the major site of cholesterolgenesis, it is the principal target organ for agents of this class. In animals, lovastatin is not as well absorbed as HA given per se, but that fraction that is absorbed reaches the portal circulation largely unchanged and is more efficiently extracted by the liver, after which it is reversibly biotransformed to HA and irreversibly to other enzymically active products. These, like HA, maintain high hepatic gradients relative to all tissues examined The minimal systemic burden for HA is attributable in part to the metabolic equilibrium, lovastatin .dblarw. HA, the opposing reactions for which appear to be present in most tissues. Excretion is very largely biliary in all species. Detailed comparisons of absorption, distribution, metabolism, and excretion profiles presented here and elsewhere indicate dogs to be the most appropriate paradigm for humans for study of lovastatin disposition.

IT 75225-51-3
RL: BIOL (Biological study)
(as lovastatin metabolite, in humans and laboratory animals)

RN 75225-51-3 HCAPLUS

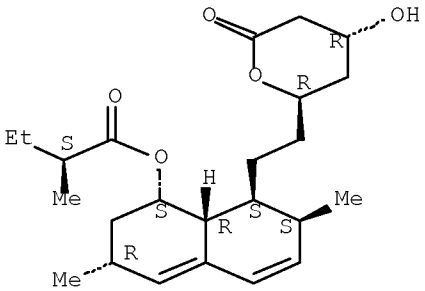
CN 1-Naphthaleneheptanoic acid, 1,2,6,7,8,8a-hexahydro-β,δ-dihydroxy-2,6-dimethyl-8-[(2S)-2-methyl-1-oxobutoxy]-, (βR,δR,1S,2S,6R,8S,8aR)- (CA INDEX NAME)

Absolute stereochemistry.



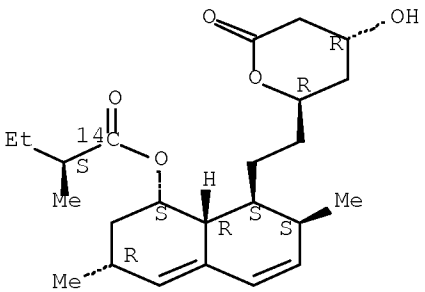
IT 75330-75-5, Lovastatin
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(metabolism of, in humans and laboratory animals)
RN 75330-75-5 HCAPLUS
CN Butanoic acid, 2-methyl-, (1S,3R,7S,8S,8aR)-1,2,3,7,8,8a-hexahydro-3,7-dimethyl-8-[2-[(2R,4R)-tetrahydro-4-hydroxy-6-oxo-2H-pyran-2-yl]ethyl]-1-naphthalenyl ester, (2S)- (CA INDEX NAME)

Absolute stereochemistry.

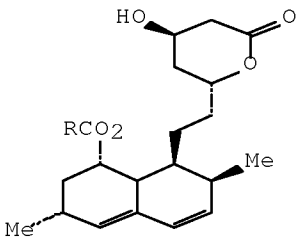


IT 120618-60-2P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and metabolism in humans and laboratory animals of)
RN 120618-60-2 HCAPLUS
CN Butanoic-1-14C acid, 2-methyl-, 1,2,3,7,8,8a-hexahydro-3,7-dimethyl-8-[2-(tetrahydro-4-hydroxy-6-oxo-2H-pyran-2-yl)ethyl]-1-naphthalenyl ester, [1S-[1α(R*),3α,7β,8β(2S*,4S*),8aβ]]- (9CI) (CA INDEX NAME)

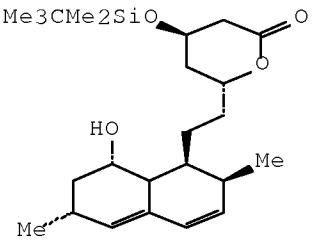
Absolute stereochemistry.



L75 ANSWER 28 OF 30 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1986:186228 HCAPLUS Full-text
DOCUMENT NUMBER: 104:186228
TITLE: 3-Hydroxy-3-methylglutaryl-coenzyme A reductase inhibitors. 4. Side-chain ester derivatives of mevinolin
AUTHOR(S): Hoffman, W. F.; Alberts, A. W.; Anderson, P. S.; Chen, J. S.; Smith, R. L.; Willard, A. K.
CORPORATE SOURCE: Merck Sharp and Dohme Res. Lab., West Point, PA, 19486, USA
SOURCE: Journal of Medicinal Chemistry (1986), 29(5), 849-52
CODEN: JMCMAR; ISSN: 0022-2623
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 104:186228
GI



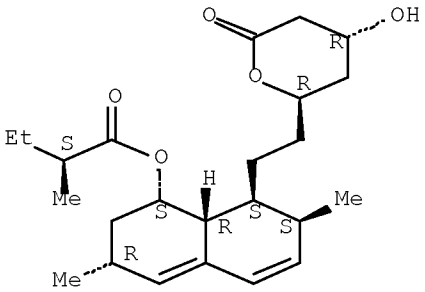
I



II

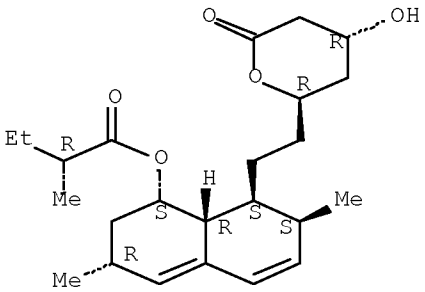
AB A series of 19 ester analogs (I) of mevinolin was prepared by acylation of the silylated alc. II by 1 of 3 developed procedures, followed by desilylation with Bu4NF-AcOH in THF. A number of the compds. (evaluated as their ring-opened Na salts) showed high anticholesteremic activity (inhibition of rat-liver HMG-CoA reductase), e.g., I (R = Me2CH, CH2:CMeCH2, CF3CHMeCH2).
IT 75330-75-5
RL: RCT (Reactant); RACT (Reactant or reagent)
(hydrolysis of)
RN 75330-75-5 HCAPLUS
CN Butanoic acid, 2-methyl-, (1S,3R,7S,8S,8aR)-1,2,3,7,8,8a-hexahydro-3,7-dimethyl-8-[2-[(2R,4R)-tetrahydro-4-hydroxy-6-oxo-2H-pyran-2-yl]ethyl]-1-naphthalenyl ester, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



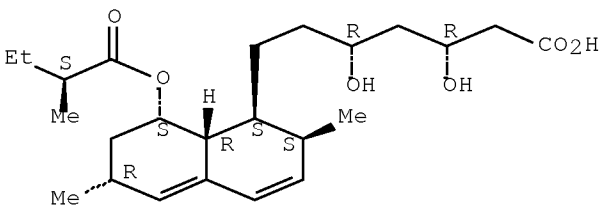
IT 79952-44-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and partial hydrolysis of)
RN 79952-44-6 HCAPLUS
CN Butanic acid, 2-methyl-, 1,2,3,7,8,8a-hexahydro-3,7-dimethyl-8-[2-(tetrahydro-4-hydroxy-6-oxo-2H-pyran-2-yl)ethyl]-1-naphthalenyl ester, [1S-[1α(S*),3α,7β,8β(2S*,4S*),8aβ]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 75225-51-3P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 75225-51-3 HCAPLUS
CN 1-Naphthaleneheptanoic acid, 1,2,6,7,8,8a-hexahydro-β,δ-dihydroxy-2,6-dimethyl-8-[(2S)-2-methyl-1-oxobutoxy]-, (βR,δR,1S,2S,6R,8S,8aR)- (CA INDEX NAME)

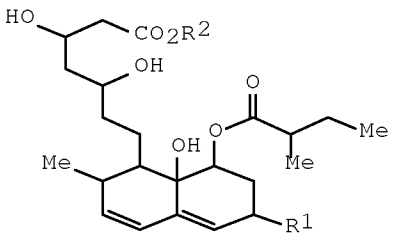
Absolute stereochemistry.



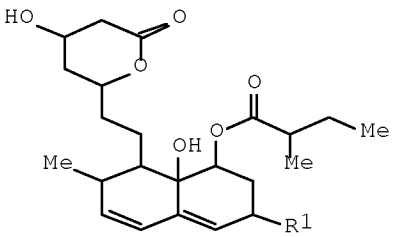
L75 ANSWER 29 OF 30 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1986:49835 HCAPLUS Full-text
DOCUMENT NUMBER: 104:49835
TITLE: Production of monacolin K and ML-236B derivatives
PATENT ASSIGNEE(S): Endo, Akira, Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 5 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 60130548	A	19850712	JP 1983-240531	19831220
JP 03055471	B	19910823		

PRIORITY APPLN. INFO.: JP 1983-240531 19831220
GI



I



II

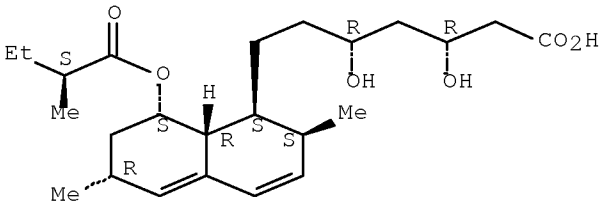
AB Monacolin K and ML-236B derivs. I and II (where R1 = H or Me; R2 = H, lower alkyl, or alkali metal) are produced with Schizophyllum species. Thus, S. commune IF04928 was cultured in a medium containing glucose 1, peptone 2, meat extract 0.1, yeast extract 0.1, and CSL 0.3% at 25° for 4 days and to this was added ML-236B Na salt (to a final concentration of 0.05%). After further cultivation at 25° for 7 days, the culture filtrate was adjusted to pH 2.0 with trifluoroacetic acid, extracted with EtOAc, and the extract was concentrated, and chromatographed to give 9-hydroxy ML-236B lactone (II, R1 = H).

IT 75225-51-3DP, derivs. 97343-98-1P
RL: BMF (Bioindustrial manufacture); BIOL (Biological study); PREP (Preparation)
(manufacture of, with Schizophyllum)

RN 75225-51-3 HCAPLUS

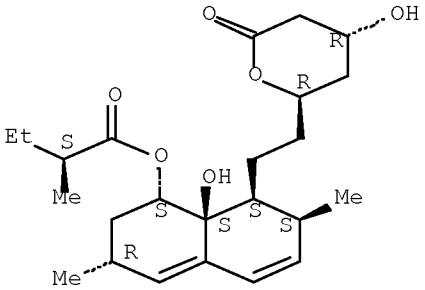
CN 1-Naphthaleneheptanoic acid, 1,2,6,7,8,8a-hexahydro-β,δ-dihydroxy-2,6-dimethyl-8-[(2S)-2-methyl-1-oxobutoxy]-, (βR,δR,1S,2S,6R,8S,8aR)- (CA INDEX NAME)

Absolute stereochemistry.



RN 97343-98-1 HCAPLUS
CN Butanoic acid, 2-methyl-, 1,2,3,7,8,8a-hexahydro-8a-hydroxy-3,7-dimethyl-8-[2-(tetrahydro-4-hydroxy-6-oxo-2H-pyran-2-yl)ethyl]-1-naphthalenyl ester, [1S-[1α(R*),3α,7β,8β(2S*,4S*),8aβ]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

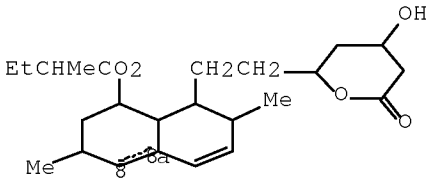


L75 ANSWER 30 OF 30 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1981:190313 HCAPLUS Full-text
DOCUMENT NUMBER: 94:190313
ORIGINAL REFERENCE NO.: 94:31139a,31142a
TITLE: Polyhydro-3,7-dimethyl-8-(2-(tetrahydro-4-hydroxy-6-oxo-2H-pyran-2-yl)-ethyl)-1-napththylenyl-2-methylbutanoates, their hydroxy acids and pharmaceutical compositions containing them
INVENTOR(S): Monaghan, Richard L.; Alberts, Alfred W.; Hoffman, Carl H.; Albers-Schonberg, George; Joshua, Henry; Lopez Aguirre, Maria B.
PATENT ASSIGNEE(S): Merck and Co., Inc., USA
SOURCE: Eur. Pat. Appl., 57 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 22478	A1	19810121	EP 1980-103286	19800612
EP 22478	B1	19830223		
R: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE				
US 4231938	A	19801104	US 1979-48946	19790615

AT 2620	T	19830315	AT 1980-103286		19800612
PRIORITY APPLN. INFO.:			US 1979-48946	A	19790615
			US 1979-77807	A	19790921
			US 1980-114459	A	19800123
			EP 1980-103286	A	19800612

OTHER SOURCE(S): MARPAT 94:190313
GI



I, 8,8a-unsatd.
II, 8,8a-satd.

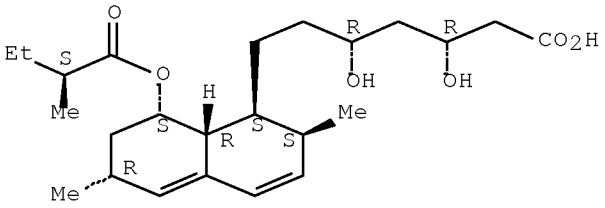
AB The title compds., which are effective in inhibiting cholesterol formation in rats, are produced by fermentation with Aspergillus terreus. Thus, A. terreus MF-4845 was inoculated into 40 mL medium (pH 7) containing dextrose 45, peptonized milk 24, autolyzed yeast 2.5 g, and polyglycol P2000 2.5 mL/L and incubated at 28° for 5 days with shaking. Total production was 21,500 units of I [75330-75-5] and II [75225-51-3]. The broth was extracted with EtOAc, the exts. were concentrated, and the solids separated by gel filtration and liquid chromatog. to yield 0.87 mg I and 3.5 mg II/10 L broth.

IT 75225-51-3P 75330-75-5P 77517-29-4P
RL: BMF (Bioindustrial manufacture); BIOL (Biological study); PREP (Preparation)
(manufacture of, with Aspergillus terreus)

RN 75225-51-3 HCAPLUS

CN 1-Naphthaleneheptanoic acid, 1,2,6,7,8,8a-hexahydro-β,δ-dihydroxy-2,6-dimethyl-8-[(2S)-2-methyl-1-oxobutoxy]-, (βR,δR,1S,2S,6R,8S,8aR)- (CA INDEX NAME)

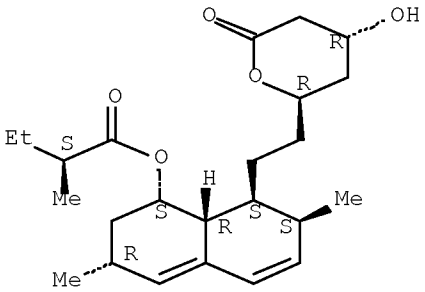
Absolute stereochemistry.



RN 75330-75-5 HCAPLUS

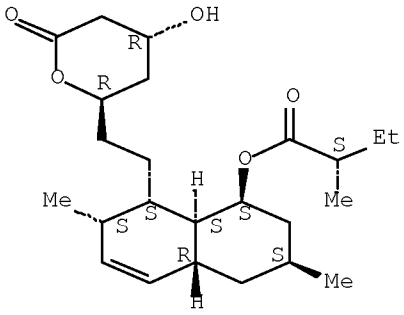
CN Butanoic acid, 2-methyl-, (1S,3R,7S,8S,8aR)-1,2,3,7,8,8a-hexahydro-3,7-dimethyl-8-[2-[(2R,4R)-tetrahydro-4-hydroxy-6-oxo-2H-pyran-2-yl]ethyl]-1-naphthalenyl ester, (2S)- (CA INDEX NAME)

Absolute stereochemistry.

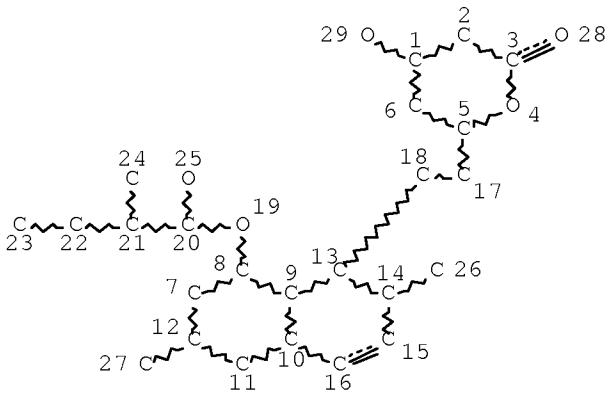


RN 77517-29-4 HCAPLUS
CN Butanoic acid, 2-methyl-, (1S,3S,4aR,7S,8S,8aS)-1,2,3,4,4a,7,8,8a-octahydro-3,7-dimethyl-8-[2-[(2R,4R)-tetrahydro-4-hydroxy-6-oxo-2H-pyran-2-yl]ethyl]-1-naphthalenyl ester, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



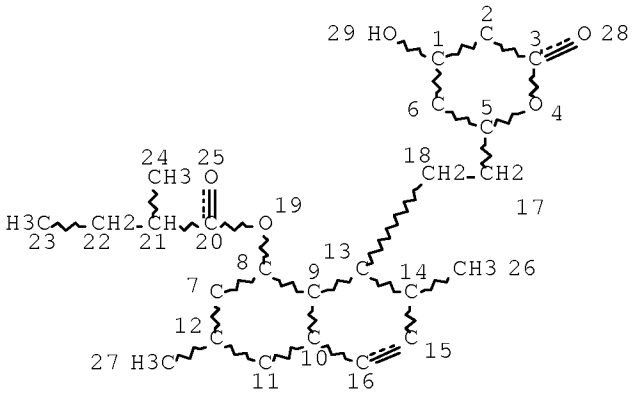
=> => D STAT QUE L91
L56 STR



NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 29

STEREO ATTRIBUTES: NONE
L58 336 SEA FILE=REGISTRY SSS FUL L56
L61 STR



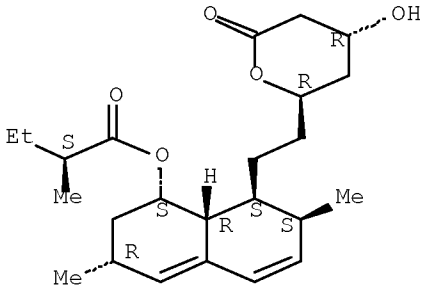
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 29

STEREO ATTRIBUTES: NONE
L63 SCR 2127
L64 33 SEA FILE=REGISTRY SUB=L58 SSS FUL L61 NOT L63
L65 3561 SEA FILE=HCAPLUS ABB=ON PLU=ON L64
L66 1 SEA FILE=REGISTRY ABB=ON PLU=ON "MEVINOLINIC ACID"/CN
L67 SEL PLU=ON L66 1- CHEM : 10 TERMS
L68 162 SEA FILE=HCAPLUS ABB=ON PLU=ON L67
L69 164 SEA FILE=HCAPLUS ABB=ON PLU=ON L68 OR MEVINOLINIC(W)ACID OR MEVINOLINATE
L70 119 SEA FILE=HCAPLUS ABB=ON PLU=ON L65 AND L69
L74 328 SEA FILE=HCAPLUS ABB=ON PLU=ON L65(L)(BMF OR PREP OR BPN)/RL

L75 30 SEA FILE=HCAPLUS ABB=ON PLU=ON L70 AND L74
L79 18 SEA FILE=REGISTRY ABB=ON PLU=ON MINERAL(L)ACID OR SULFONIC ACID/CN OR NITRIC ACID/CN OR ORTHOPHOSPHORIC ACID/CN OR HYDROCHLORIC ACID/CN
L80 1 SEA FILE=REGISTRY ABB=ON PLU=ON ORTHOPHOSPHORIC ACID/CN
L81 72933 SEA FILE=HCAPLUS ABB=ON PLU=ON L80
L82 399316 SEA FILE=HCAPLUS ABB=ON PLU=ON L79 OR (MINERAL OR SULFURIC OR NITRIC OR L81 OR HYDROCHLORIC)(W) ACID
L83 15 SEA FILE=HCAPLUS ABB=ON PLU=ON L74 AND L82
L84 1388 SEA FILE=REGISTRY ABB=ON PLU=ON SOLVENT OR SOLVENTS OR HYDROCARBONS/CN
L86 1959522 SEA FILE=HCAPLUS ABB=ON PLU=ON L83 OR L84 OR SOLVENT OR HYDROCARBON OR ?DICHLOROMETHANE OR CHLOROFORM OR ISOPROPANOL

```
                OR ALUMINA OR ACETONE
L87          233 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L65 AND L86
L88           48 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L87 AND L74
L89           80 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L65 AND (FILT? OR ?CRYSTALI?
                OR EVAPORA?)
L90           29 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L89 AND L74
L91           45 SEA FILE=HCAPLUS ABB=ON  PLU=ON  (L83 OR L88 OR L90) NOT L75


=> D IBIB ABS HITSTR L91 1-45

L91  ANSWER 1 OF 45  HCAPLUS  COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER:         2007:284157  HCAPLUS  Full-text
DOCUMENT NUMBER:          146:337726
TITLE:                    Process for preparation of lactones and Atorvastatin
                          calcium salt
INVENTOR(S):              Aslan, Tuncer; Uensal, Serafettin
PATENT ASSIGNEE(S):       Ulkar Kimya Sanayii ve Ticaret A.S., Turk.
SOURCE:                   PCT Int. Appl., 28pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.           KIND   DATE        APPLICATION NO.         DATE
     ---------------      ----   --------    --------------------    --------
     WO 2007028412         A1    20070315    WO 2005-EP9740          20050910
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
             CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
             GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ,
             LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA,
             NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK,
             SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU,
             ZA, ZM, ZW
         RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
             IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ,
             CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH,
             GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
             KG, KZ, MD, RU, TJ, TM
PRIORITY APPLN. INFO.:                       WO 2005-EP9740          20050910
OTHER SOURCE(S):          CASREACT 146:337726; MARPAT 146:337726
AB    This invention pertains to a method for preparation of Atorvastatin lactone
      and Atorvastatin calcium salt, which comprises hydrolysis of Atorvastatin. For
      example, a protected Atorvastatin compound was hydrolyzed with HONH2•HCl in
      mixed solvent to give Atorvastatin lactone.  The Atorvastatin lactone was
      treated with NaOH, followed by the addition of Ca(OH)2 to provide the title
      Atorvastatin calcium salt.
IT    75330-75-5P, Lovastatin lactone
      RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic
      preparation); PREP (Preparation); RACT (Reactant or reagent)
         (preparation of lactones and Atorvastatin calcium salt)
RN    75330-75-5  HCAPLUS
CN    Butanoic acid, 2-methyl-, (1S,3R,7S,8S,8aR)-1,2,3,7,8,8a-hexahydro-3,7-
      dimethyl-8-[2-[(2R,4R)-tetrahydro-4-hydroxy-6-oxo-2H-pyran-2-yl]ethyl]-1-
      naphthalenyl ester, (2S)-  (CA INDEX NAME)

Absolute stereochemistry.
```



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L91 ANSWER 2 OF 45 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:1084937 HCAPLUS Full-text
DOCUMENT NUMBER: 146:58286
TITLE: Monascus sp. mutants having excellent monacolin k production capacity and cholesterol inhibitor comprising extract thereof
INVENTOR(S): Hwang, Han Joon; Suh, Soo Hwan
PATENT ASSIGNEE(S): Korea University Industry and Academy Cooperation Foundation, S. Korea
SOURCE: Repub. Korean Kongkae Taeho Kongbo, No pp. given
CODEN: KRXXA7
DOCUMENT TYPE: Patent
LANGUAGE: Korean
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

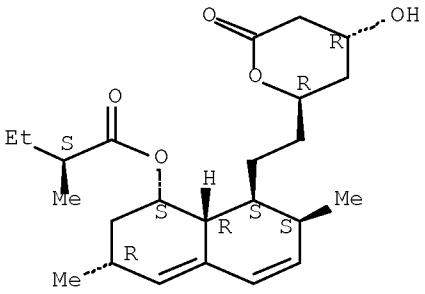
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
KR 2006021769	A	20060308	KR 2004-70647	20040904
PRIORITY APPLN. INFO.:			KR 2004-70647	20040904

AB A Monascus sp. mutant is provided to produce monacolin K having excellent inhibition capacity against cholesterol synthesis, not produce mycotoxin such as citrinin and have improved productivity of red pigment, thereby being applied as a cholesterol inhibition agent or functional food. The Monascus sp. mutant is deposited as KCCM 10586, produces Monacolin K with high efficiency, and does not produce citrinin. The Monasus sp. mutant is cultured in a culture medium including 2-3% of soytone, 2-3% of glucose, 0.04-0.06 g of MgSO4, and 75-85% of wheat flour. The cholesterol inhibitor comprises extract of the Monasus sp. mutant containing Monacolin K.

IT 75330-75-5P, Monacolin k
RL: BMF (Bioindustrial manufacture); BIOL (Biological study); PREP (Preparation)
(Monasus sp. mutants having excellent monacolin k production capacity and cholesterol inhibitor comprising extract thereof)

RN 75330-75-5 HCAPLUS
CN Butanoic acid, 2-methyl-, (1S,3R,7S,8S,8aR)-1,2,3,7,8,8a-hexahydro-3,7-dimethyl-8-[2-[(2R,4R)-tetrahydro-4-hydroxy-6-oxo-2H-pyran-2-yl]ethyl]-1-naphthalenyl ester, (2S)- (CA INDEX NAME)

Absolute stereochemistry.

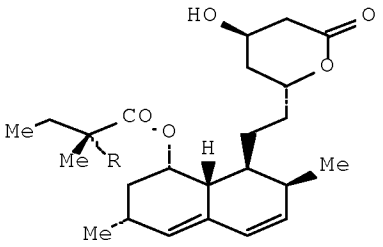


L91 ANSWER 3 OF 45 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:544581 HCAPLUS Full-text
DOCUMENT NUMBER: 145:27768
TITLE: An improved process for lactonization to produce highly pure statins
INVENTOR(S): Suri, Sanjay; Kashyap, Tapan; Pundir, Girish Chandra
PATENT ASSIGNEE(S): Morepen Laboratories Ltd., India
SOURCE: PCT Int. Appl., 11 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

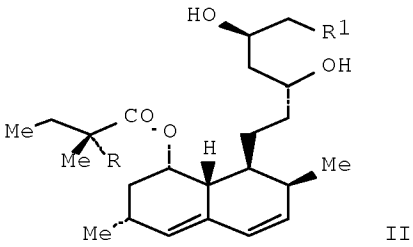
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006059346	A2	20060608	WO 2005-IN392	20051130
WO 2006059346	A3	20060908		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: IN 2004-DE2401 A 20041201
OTHER SOURCE(S): CASREACT 145:27768; MARPAT 145:27768
GI



I



II

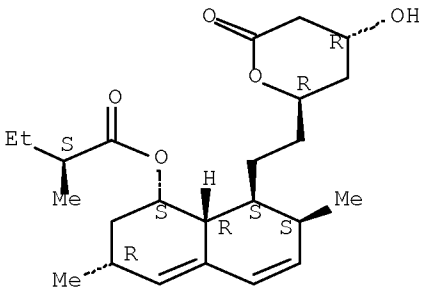
AB A process was disclosed for preparation of a statin I (R = H, Me) via lactonization of a corresponding statin hydroxyacid or its salts II (R = H, Me; R1 = CO2H, CO2-.M+; M = metal cation, N+H4) that avoids use of strong corrosive acids and drastic heat conditions. Specifically, the process can be carried out at moderate temperature resulting in statins particularly simvastatin I (R = Me) with purity greater than 99% and dimer impurity to a level of less than 0.05%. The process involves using a mixture of carboxylic acid anhydride and water miscible organic solvent. Specifically, the reagents used may be acetic anhydride and acetonitrile. The statin is precipitated using water and further purified if so desired.

IT 75330-75-5P, Lovastatin
RL: PUR (Purification or recovery); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(claimed compound; improved process for lactonization to produce highly pure statins)

RN 75330-75-5 HCAPLUS

CN Butanoic acid, 2-methyl-, (1S,3R,7S,8S,8aR)-1,2,3,7,8,8a-hexahydro-3,7-dimethyl-8-[2-[(2R,4R)-tetrahydro-4-hydroxy-6-oxo-2H-pyran-2-yl]ethyl]-1-naphthalenyl ester, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



L91 ANSWER 4 OF 45 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:318694 HCAPLUS Full-text
DOCUMENT NUMBER: 144:350442
TITLE: Crystallization process for the purification of lovastatin by removing dihydrolovastatin
INVENTOR(S): Kumar, Parveen; Mitra, Ashoke; Malviya, Hitesh, Kumar
PATENT ASSIGNEE(S): Ranbaxy Laboratories Limited, India
SOURCE: PCT Int. Appl., 14 pp.

CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006035295	A1	20060406	WO 2005-IB2863	20050927

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

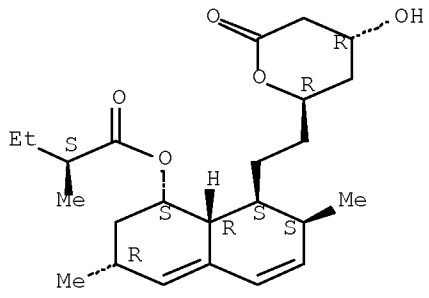
PRIORITY APPLN. INFO.: IN 2004-DE1850 A 20040927

AB A crystallization process for the preparation of lovastatin substantially free of dihydrolovastatin is described which may be used for treating hypercholesterolemia.

IT 75330-75-5P, Lovastatin
RL: NPO (Natural product occurrence); PEP (Physical, engineering or chemical process); PUR (Purification or recovery); PYP (Physical process); BIOL (Biological study); OCCU (Occurrence); PREP (Preparation); PROC (Process)
(crystallization process for the purification of lovastatin by removing dihydrolovastatin)

RN 75330-75-5 HCAPLUS
CN Butanoic acid, 2-methyl-, (1S,3R,7S,8S,8aR)-1,2,3,7,8,8a-hexahydro-3,7-dimethyl-8-[2-[(2R,4R)-tetrahydro-4-hydroxy-6-oxo-2H-pyran-2-yl]ethyl]-1-naphthalenyl ester, (2S)- (CA INDEX NAME)

Absolute stereochemistry.

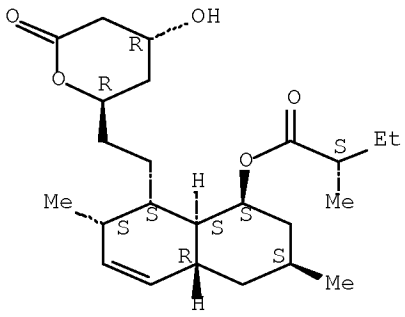


IT 77517-29-4, Dihydrolovastatin
RL: PEP (Physical, engineering or chemical process); PYP (Physical process); REM (Removal or disposal); PROC (Process)
(crystallization process for the purification of lovastatin by removing dihydrolovastatin)

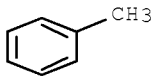
RN 77517-29-4 HCAPLUS

CN Butanoic acid, 2-methyl-, (1S,3S,4aR,7S,8S,8aS)-1,2,3,4,4a,7,8,8a-octahydro-3,7-dimethyl-8-[2-[(2R,4R)-tetrahydro-4-hydroxy-6-oxo-2H-pyran-2-yl]ethyl]-1-naphthalenyl ester, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



IT 108-88-3, Toluene, uses
RL: NUU (Other use, unclassified); USES (Uses)
(solvent; crystallization process for the purification of lovastatin by removing dihydrolovastatin using)
RN 108-88-3 HCAPLUS
CN Benzene, methyl- (CA INDEX NAME)



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L91 ANSWER 5 OF 45 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:308708 HCAPLUS Full-text
DOCUMENT NUMBER: 144:398246
TITLE: Method for manufacturing Monascus purpureus extract with increased content of statins
INVENTOR(S): Li, Chaohui
PATENT ASSIGNEE(S): Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing Gongkai Shuomingshu, 7 pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 1742755	A	20060308	CN 2005-10011056	20051011

PRIORITY APPLN. INFO.: CN 2005-10011056 20051011

AB The title method comprises: (1) extracting crude drug or decoction tablet of Monascus purpureus under 40-90℃ with 2-5 times of 40-85% solvent, filtering, (2) concentrating, adding one or more powder solid substances, and (3) drying

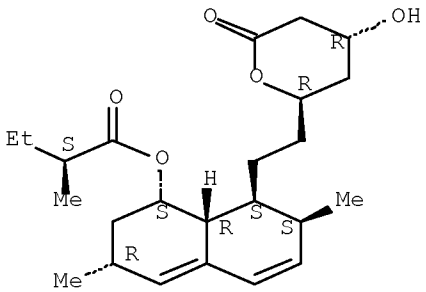
until the water content is less than 5%, and pulverizing. This method can greatly reduce the content of starch ingredient in the Monascus purpureus extract and increase the content of statins active ingredient.

IT 75330-75-5P, Lovastatin
RL: PAC (Pharmacological activity); PUR (Purification or recovery); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(method for manufacturing Monascus purpureus extract with increased content of statins)

RN 75330-75-5 HCAPLUS

CN Butanoic acid, 2-methyl-, (1S,3R,7S,8S,8aR)-1,2,3,7,8,8a-hexahydro-3,7-dimethyl-8-[2-[(2R,4R)-tetrahydro-4-hydroxy-6-oxo-2H-pyran-2-yl]ethyl]-1-naphthalenyl ester, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



L91 ANSWER 6 OF 45 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2006:225505 HCAPLUS Full-text

DOCUMENT NUMBER: 145:291148

TITLE: Production of statins through solid fermentation

AUTHOR(S): Trisnamurti, R. H.; Udin, L. Z.; Hanafi, M.; Kardono, L. B. S.

CORPORATE SOURCE: Research Center for Chemistry, Indonesian Institute of Sciences, Bandung, 40135, Indonesia

SOURCE: World Congress of Chemical Engineering, 7th, Glasgow, United Kingdom, July 10-14, 2005 (2005), 85785/1-85785/10. Institution of Chemical Engineers: Rugby, UK.
CODEN: 69HUFZ; ISBN: 0-85295-494-8

DOCUMENT TYPE: Conference; (computer optical disk)

LANGUAGE: English

AB Twenty-five per cent of the adult population is thought to have elevated cholesterol levels (above 200-240mg.). The "statin" drugs are used to prevent cardiovascular disease, specifically by decreasing the accumulation of cholesterol plaques on vascular walls of coronary and carotid arteries. Lovastatin, simvastatin and other derivs. have been produced through solid fermentation using Aspergillus sp., followed by chemical conversion. The fermentation duration was conducted for 5 days, using various media. Semi-pilot production to produced 0.5 to 1 kg lovastatin per batch will be conducted. Various difficulties encountered especially in maintaining the aseptic condition during the fermentation course. Abundant fermentation solid waste has also been found. The residue obtained from the lovastatin

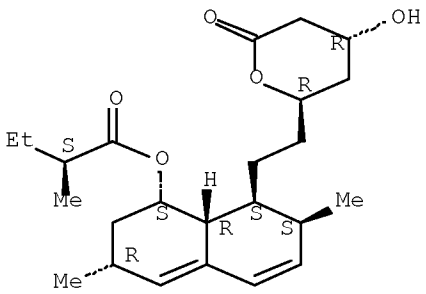
extraction with organic solvent exhibited α-glucosidase inhibitory activity. This may give opportunities for development of anti-diabetic drug. Following the work on extract residue, several secondary metabolites have been isolated and identified.

IT 75330-75-5P, Lovastatin
RL: BMF (Bioindustrial manufacture); PUR (Purification or recovery); BIOL (Biological study); PREP (Preparation)
(solid fermentation using γ-irradiated Aspergillus terreus show high lovastatin in mutant A4B3 than wild type and lovastatin residue with organic solvent exhibited α-glucosidase inhibitory activity)

RN 75330-75-5 HCAPLUS

CN Butanoic acid, 2-methyl-, (1S,3R,7S,8S,8aR)-1,2,3,7,8,8a-hexahydro-3,7-dimethyl-8-[2-[(2R,4R)-tetrahydro-4-hydroxy-6-oxo-2H-pyran-2-yl]ethyl]-1-naphthalenyl ester, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L91 ANSWER 7 OF 45 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:1204874 HCAPLUS Full-text
DOCUMENT NUMBER: 143:435393
TITLE: Method for extracting and refining lovastatin
INVENTOR(S): Song, Aigang; Sun, Mei; Zhou, Xiongbing; Qin, Yongzhong; Qin, Najia
PATENT ASSIGNEE(S): Shandong Lukang Pharmaceutical Co., Ltd., Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing Gongkai Shuomingshu, 7 pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

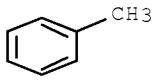
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 1583736	A	20050223	CN 2004-10024183	20040603

PRIORITY APPLN. INFO.: CN 2004-10024183 20040603

AB The invention relates to a method for extracting and refining lovastatin from lovastatin enriched fermentation liquor generated from Aspergillus terreus cultivation with resin. The method comprises (1) alkalizing the fermentation liquor to form lovastatin salt and release the salt from spore inside to spore

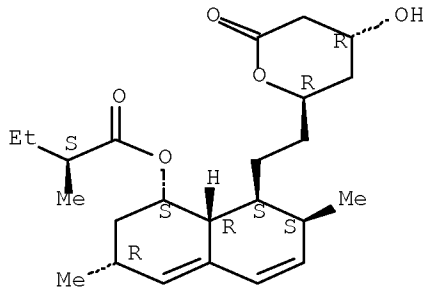
outside, and filtrating; (2) carrying out adsorption extraction of the lovastatin in the filtrate with resin; (3) concentrating for cyclization and crystallization; (4) centrifuging, washing, and drying to obtain the crude product; and (5) recrystg. to obtain the final product. With this method, qualified lovastatin product can be obtained by using a small amount of solvent. The method has the advantages of simple operation, high yield, low cost, and easy application.

IT 108-88-3, Toluene, uses
RL: NUU (Other use, unclassified); USES (Uses)
(method for extracting and refining lovastatin)
RN 108-88-3 HCAPLUS
CN Benzene, methyl- (CA INDEX NAME)



IT 75330-75-5P, Lovastatin
RL: PEP (Physical, engineering or chemical process); PUR (Purification or recovery); PYP (Physical process); PREP (Preparation); PROC (Process)
(method for extracting and refining lovastatin)
RN 75330-75-5 HCAPLUS
CN Butanoic acid, 2-methyl-, (1S,3R,7S,8S,8aR)-1,2,3,7,8,8a-hexahydro-3,7-dimethyl-8-[2-[(2R,4R)-tetrahydro-4-hydroxy-6-oxo-2H-pyran-2-yl]ethyl]-1-naphthalenyl ester, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



L91 ANSWER 8 OF 45 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:1196551 HCAPLUS Full-text
DOCUMENT NUMBER: 143:439101
TITLE: Edible oil containing statins
INVENTOR(S): Beindorff, Christiaan Michaeel; Meijer, Willem Maarten; Molhuizen, Henricus Otto Franciscus
PATENT ASSIGNEE(S): Unilever N. V., Neth.; Unilever PLC; Hindustan Lever Limited
SOURCE: PCT Int. Appl., 32 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent

LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005104864	A1	20051110	WO 2005-EP3246	20050323
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2005237213	A1	20051110	AU 2005-237213	20050323
CA 2563128	A1	20051110	CA 2005-2563128	20050323
EP 1740056	A1	20070110	EP 2005-716408	20050323
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR				
CN 1946302	A	20070411	CN 2005-80012636	20050323
BR 2005009422	A	20070904	BR 2005-9422	20050323
JP 2007534328	T	20071129	JP 2007-509905	20050323
MX 2006PA12251	A	20061215	MX 2006-PA12251	20061023
IN 2006MN01260	A	20070608	IN 2006-MN1260	20061027
US 2007218185	A1	20070920	US 2006-587726	20061027
PRIORITY APPLN. INFO.:			EP 2004-76293 A	20040428
			WO 2005-EP3246 W	20050323

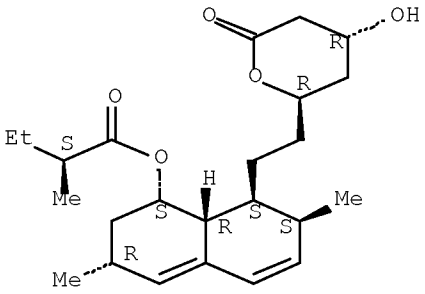
AB An edible oil (≥90% di- and/or triglycerides with a saturated fatty acid content <25 wt%) may contain statins for incorporation in food products. The edible oil is obtained by supercrit. extraction of a substrate which is fermented with a statin-producing fungus. Thus, soybean oil containing 1 mg lovastatin/g (obtained by fermentation of soybeans with Monascus ruber) is incorporated into bovine milk.

IT 75330-75-5P, Lovastatin
RL: BMF (Bioindustrial manufacture); FFD (Food or feed use); PUR (Purification or recovery); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(edible oil containing statins)

RN 75330-75-5 HCAPLUS

CN Butanoic acid, 2-methyl-, (1S,3R,7S,8S,8aR)-1,2,3,7,8,8a-hexahydro-3,7-dimethyl-8-[2-[(2R,4R)-tetrahydro-4-hydroxy-6-oxo-2H-pyran-2-yl]ethyl]-1-naphthalenyl ester, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L91 ANSWER 9 OF 45 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:1196120 HCAPLUS Full-text
DOCUMENT NUMBER: 143:439126
TITLE: Flour-based food product comprising statins
INVENTOR(S): Beindorff, Christiaan Michaeel; Meijer, Willem Maarten; Molhuizen, Henricus Otto Franciscus
PATENT ASSIGNEE(S): Unilever N. V., Neth.; Unilever PLC; Hindustan Lever Limited
SOURCE: PCT Int. Appl., 29 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005104871	A1	20051110	WO 2005-EP3247	20050323
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2005237214	A1	20051110	AU 2005-237214	20050323
CA 2563153	A1	20051110	CA 2005-2563153	20050323
EP 1740061	A1	20070110	EP 2005-716409	20050323
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR				
CN 1946304	A	20070411	CN 2005-80012633	20050323
BR 2005009437	A	20070904	BR 2005-9437	20050323
JP 2007534708	T	20071129	JP 2007-509906	20050323
MX 2006PA12250	A	20061215	MX 2006-PA12250	20061023
IN 2006MN01261	A	20070608	IN 2006-MN1261	20061027

PRIORITY APPLN. INFO.:	EP 2004-76293	A	20040428
	EP 2004-77219	A	20040803
	WO 2005-EP3247	W	20050323

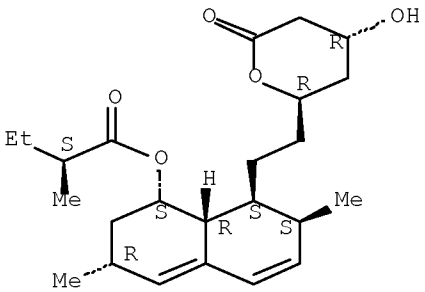
AB A flour (<10 weight% fat) is used in combination with statins for preparation of a food product. A substrate is fermented with a statin-producing fungus and fat in the substrate is extracted Thus, a defatted soybean flour containing 1 mg statins/g (obtained by fermentation of soybeans with Monascus ruber) is incorporated in low-fat oat pancakes or raisin bread.

IT 75330-75-5P, Lovastatin
RL: BMF (Bioindustrial manufacture); FFD (Food or feed use); PUR (Purification or recovery); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(flour-based food product comprising statins)

RN 75330-75-5 HCAPLUS

CN Butanoic acid, 2-methyl-, (1S,3R,7S,8S,8aR)-1,2,3,7,8,8a-hexahydro-3,7-dimethyl-8-[2-[(2R,4R)-tetrahydro-4-hydroxy-6-oxo-2H-pyran-2-yl]ethyl]-1-naphthalenyl ester, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L91 ANSWER 10 OF 45 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:1103765 HCAPLUS Full-text
DOCUMENT NUMBER: 143:392909
TITLE: An improved method for manufacture of 4-hydroxypyran-2-one derivatives
INVENTOR(S): Gharpure, Milind Moreshwar; Sonawane, Swapnil Panditrao; Mane, Srihari Shivaji; Mahale, Rajendra Dattatreya
PATENT ASSIGNEE(S): Lupin Ltd., India
SOURCE: PCT Int. Appl., 43 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

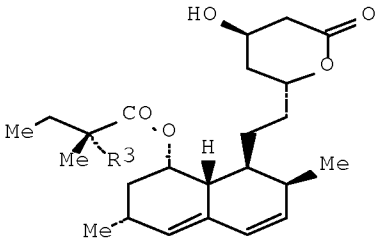
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005095374	A1	20051013	WO 2004-IN75	20040330

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

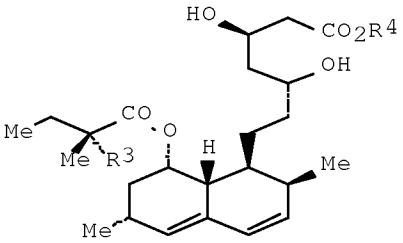
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

AU 2004317826	A1	20051013	AU 2004-317826	20040330
EP 1732912	A1	20061220	EP 2004-770635	20040330
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LI, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, MK				
BR 2004018644	A	20070529	BR 2004-18644	20040330
IN 2006MN01137	A	20070608	IN 2006-MN1137	20060925
PRIORITY APPLN. INFO.:			WO 2004-IN75 A	20040330

GI



I



II

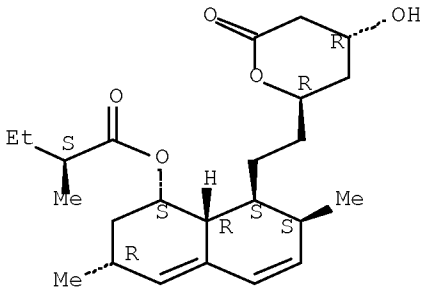
AB A process for preparation, crystallization, and purification of anti-hypercholesterolemic agents, such as I (R3 = H, Me) containing a 4-hydroxypyran-2-one moiety, was disclosed. The process comprised heating a corresponding open-chain acid II (R4 = H, N+H4, alkali metal) in a solvent mixture consisting of an aromatic hydrocarbon and a ketone in an inert atmospheric at a temperature of between 60℃ to 92℃ in the absence or presence of orthophosphoric acid or its alkali dihydrogen salts or alkali hydrogen salts of a dibasic acid, followed by optional neutralization of the reaction mixture with an organic base and obtaining the desired 4-hydroxypyran-2-ones I in high purity and substantially free of impurities through a step of isolation and crystallization This process leads to formation of derivs. I in high purity with dimer impurity less than 0.1% and anhydro impurity below 0.15%. Thus, simvastatin ammonium salt II (R3 = Me, R4 = N+H4) in toluene and Me Et ketone was treated with orthophosphoric acid to give simvastatin I (R3 = Me) in 67.3% yield and 99.7% purity.

IT 75330-75-5P, Lovastatin
RL: IMF (Industrial manufacture); PUR (Purification or recovery); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(improved method for preparation, crystallization, and purification of 4-hydroxypyran-2-one derivs., such as simvastatin and lovastatin)

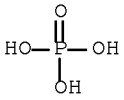
RN 75330-75-5 HCAPLUS

CN Butanoic acid, 2-methyl-, (1S,3R,7S,8S,8aR)-1,2,3,7,8,8a-hexahydro-3,7-dimethyl-8-[2-[(2R,4R)-tetrahydro-4-hydroxy-6-oxo-2H-pyran-2-yl]ethyl]-1-naphthalenyl ester, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



IT 7664-38-2, Orthophosphoric acid, reactions
RL: RGT (Reagent); RACT (Reactant or reagent)
(improved method for preparation, crystallization, and purification of 4-hydroxypyran-2-one derivs., such as simvastatin and lovastatin)
RN 7664-38-2 HCAPLUS
CN Phosphoric acid (CA INDEX NAME)



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L91 ANSWER 11 OF 45 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:520094 HCAPLUS Full-text
DOCUMENT NUMBER: 143:6410
TITLE: Process for the recovery and purification of lovastatin from fermentation broth
INVENTOR(S): Asensio Dominguez, Ramon; Cruzado Rodriguez, Ma. Carmen; Diaz Tejo, Luis Angel; Requena Perez, Felipe; Perez de Las Heras, Jose Maria
PATENT ASSIGNEE(S): Ercros Industrial, S.A., Spain
SOURCE: Span., 12 pp.
CODEN: SPXXAD
DOCUMENT TYPE: Patent
LANGUAGE: Spanish
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
ES 2204285	A1	20040416	ES 2002-1145	20020520
ES 2204285	B1	20050301		
PRIORITY APPLN. INFO.:			ES 2002-1145	20020520

AB A process for the recovery and purification of lovastatin (I) from fermentation broth comprises: (A) precipitation of I by adjusting the pH of the broth to an acid value by the addition of acid (e.g., HCl); (B) separating the I by filtration; (C) dissolving the recovered I in dichloromethane; (D)

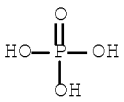
concentrating the I by the removal of dichloromethane; (E) crystallizing the I in xylene; and (F) purifying the obtained I.

IT 7647-01-0, Hydrogen chloride, reactions 7664-38-2, Phosphoric acid, reactions
RL: RGT (Reagent); RACT (Reactant or reagent)
(in a process for the recovery and purification of lovastatin from fermentation broth)

RN 7647-01-0 HCAPLUS
CN Hydrochloric acid (CA INDEX NAME)

HCl

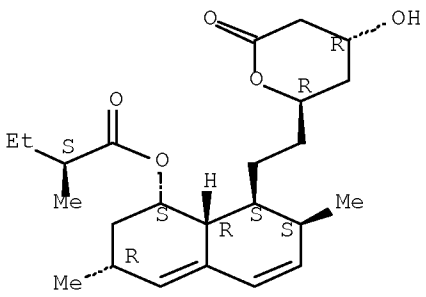
RN 7664-38-2 HCAPLUS
CN Phosphoric acid (CA INDEX NAME)



IT 75330-75-5P, Lovastatin
RL: BMF (Bioindustrial manufacture); PEP (Physical, engineering or chemical process); PUR (Purification or recovery); PYP (Physical process); BIOL (Biological study); PREP (Preparation); PROC (Process)
(process for the recovery and purification of lovastatin from fermentation broth)

RN 75330-75-5 HCAPLUS
CN Butanoic acid, 2-methyl-, (1S,3R,7S,8S,8aR)-1,2,3,7,8,8a-hexahydro-3,7-dimethyl-8-[2-[(2R,4R)-tetrahydro-4-hydroxy-6-oxo-2H-pyran-2-yl]ethyl]-1-naphthalenyl ester, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



L91 ANSWER 12 OF 45 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:435164 HCAPLUS Full-text

DOCUMENT NUMBER: 144:231571
TITLE: Enhanced Monacolin K production of Monascus ruber by adding yeast lysate
AUTHOR(S): Zhao, Shuxin; Tang, Weihua; Qiao, Changsheng
CORPORATE SOURCE: College of Food Science and Bioengineering, Tianjin University of Science and Technology, Tianjin, 300222, Peop. Rep. China
SOURCE: Shipin Kexue (Beijing, China) (2004), 25(4), 119-121
CODEN: SPKHD5; ISSN: 1002-6630
PUBLISHER: Zhongguo Shipin Zazhishe
DOCUMENT TYPE: Journal
LANGUAGE: Chinese

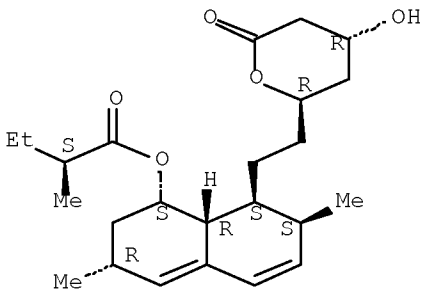
AB During the fermentation of Monascus ruber, adding yeast lysate, yeast and yeast broth filtrate can improve the yield of Monacolin K. The yield of Monacolin K cultured with yeast lysate, yeast and yeast broth filtrate is 48.06, 43.64 and 44.79 mg/L, resp., compared with Monascus cultured without inducer, increase 1.38, 1.26 and 1.29 times, resp. Adding Yeast lysate in the beginning of Monascus fermentation by the quantity of 2.67% (volume/volume), the yield of Monacolin K reaches 61.99 mg/L. Study on the variance of Monascus biomass show yeast lysate could improve the biomass of Monascus and metabolize pathway, so increase the yield of Monacolin K.

IT 75330-75-5P, Monacolin K
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); BIOL (Biological study); PREP (Preparation)
(enhanced Monacolin K production by Monascus ruber by adding yeast lysate)

RN 75330-75-5 HCAPLUS

CN Butanoic acid, 2-methyl-, (1S,3R,7S,8S,8aR)-1,2,3,7,8,8a-hexahydro-3,7-dimethyl-8-[2-[(2R,4R)-tetrahydro-4-hydroxy-6-oxo-2H-pyran-2-yl]ethyl]-1-naphthalenyl ester, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



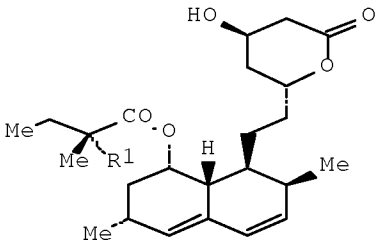
L91 ANSWER 13 OF 45 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:195668 HCAPLUS Full-text
DOCUMENT NUMBER: 142:219081
TITLE: An improved process for the preparation of statins
INVENTOR(S): Kumar, Yatendra; Thaper, Rajesh Kumar; Kumar, S. M. Dileep; Khanna, Jag Mohan
PATENT ASSIGNEE(S): Ranbaxy Laboratories Limited, India
SOURCE: Indian, 9 pp.
CODEN: INXXAP
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

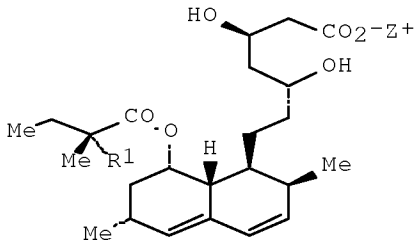
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
IN 186879	A1	20011201	IN 1997-DE3101	19971028

PRIORITY APPLN. INFO.: IN 1997-DE3101 19971028

GI



I



II

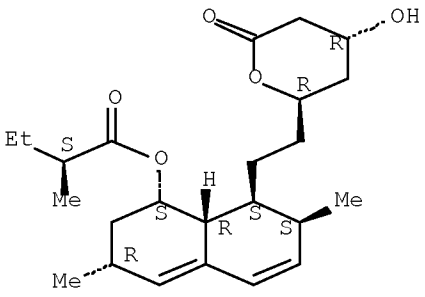
AB A process for the preparation of statins I (R1 = H, Me) was disclosed and comprised lactonization of mevinic acid or its analogs II (R1 = H, Me, Z = Na, K, NH4) by heating in organic solvent, from about ambient temperature to reflux of the solvents under anhydrous conditions in the presence of a mild catalyst and precipitating the product by addition of water and collecting the crystalline product from the mixture

IT 75330-75-5P, Lovastatin
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(claimed compound; process for the preparation of statins via lactonization)

RN 75330-75-5 HCAPLUS

CN Butanoic acid, 2-methyl-, (1S,3R,7S,8S,8aR)-1,2,3,7,8,8a-hexahydro-3,7-dimethyl-8-[2-[(2R,4R)-tetrahydro-4-hydroxy-6-oxo-2H-pyran-2-yl]ethyl]-1-naphthalenyl ester, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



L91 ANSWER 14 OF 45 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2004:1127534 HCAPLUS Full-text

DOCUMENT NUMBER: 142:54837

TITLE: Ion-exchange filtration of fermentation broth

INVENTOR(S): Keri, Vilmos; Melczer, Istvan; Deak, Lajos; Szeles, Krisztian
PATENT ASSIGNEE(S): Biogal Gyogyszergyar Rt., Hung.; Teva Pharmaceuticals USA, Inc.
SOURCE: PCT Int. Appl., 15 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004111255	A1	20041223	WO 2004-US18633	20040609
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2005003499	A1	20050106	US 2004-865590	20040609

PRIORITY APPLN. INFO.: US 2003-477102P P 20030609

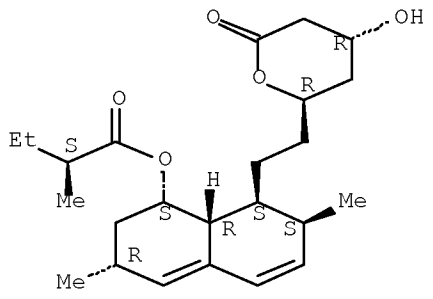
AB The invention encompasses a process for purifying a fermentation broth by providing a fermentation broth, adjusting the pH of the fermentation broth, isolating a filtrate from the fermentation broth, and passing the filtrate through a cation-exchange resin to obtain a purified filtrate.

IT 75330-75-5P, Lovastatin
RL: BMF (Bioindustrial manufacture); PUR (Purification or recovery); BIOL (Biological study); PREP (Preparation)
(ion-exchange filtration of fermentation broth)

RN 75330-75-5 HCAPLUS

CN Butanoic acid, 2-methyl-, (1S,3R,7S,8S,8aR)-1,2,3,7,8,8a-hexahydro-3,7-dimethyl-8-[2-[(2R,4R)-tetrahydro-4-hydroxy-6-oxo-2H-pyran-2-yl]ethyl]-1-naphthalenyl ester, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



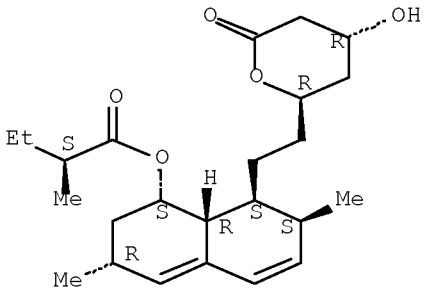
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L91 ANSWER 15 OF 45 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:853870 HCAPLUS Full-text
DOCUMENT NUMBER: 142:79904
TITLE: Process for producing lovastatin
INVENTOR(S): Kim, Jung Woo; Kim, Kyung Hwan; Lee, Sang Chul; Ham, Yun Beam
PATENT ASSIGNEE(S): Jongkundnag Co., Ltd., S. Korea
SOURCE: Repub. Korea, No pp. given
CODEN: KRXXFC
DOCUMENT TYPE: Patent
LANGUAGE: Korean
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
KR 200243	B1	19990615	KR 1995-17251	19950624
PRIORITY APPLN. INFO.:			KR 1995-17251	19950624

AB A production process of lovastatin is provided which uses single alumina chromatog. so that it is profitable in terms of process and environmental protection. The production process of lovastatin comprises the steps: (i) extraction of Aspergillus terreus culture using Et acetate, (ii) adsorbing the concentrated extract on an alumina column and elution; and (iii) drying and then adding anhydrous alc. solvent to crystallize.
IT 75330-75-5P, Lovastatin
RL: PUR (Purification or recovery); PREP (Preparation)
(process for producing robastatin from Aspergillus terreus culture)
RN 75330-75-5 HCAPLUS
CN Butanoic acid, 2-methyl-, (1S,3R,7S,8S,8aR)-1,2,3,7,8,8a-hexahydro-3,7-dimethyl-8-[2-[(2R,4R)-tetrahydro-4-hydroxy-6-oxo-2H-pyran-2-yl]ethyl]-1-naphthalenyl ester, (2S)- (CA INDEX NAME)

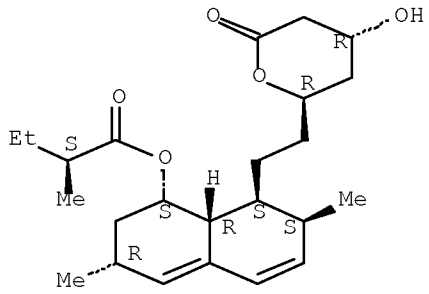
Absolute stereochemistry.



L91 ANSWER 16 OF 45 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:577260 HCAPLUS Full-text
DOCUMENT NUMBER: 142:296720
TITLE: The Determination of Monacolin K in Fermentation Samples of Monascus sp. by HPLC
AUTHOR(S): Jia, Bo; Sun, Baishen; Zhou, Liping
CORPORATE SOURCE: College of Biological and Environmental Engineering, Zhejiang University of Technology, Hangzhou, 310014, Peop. Rep. China
SOURCE: Shipin Yu Fajiao Gongye (2003), 29(1), 70-72, 82

CODEN: SPYYDO; ISSN: 0253-990X
PUBLISHER: Shipin Yu Fajiao Gongye
DOCUMENT TYPE: Journal
LANGUAGE: Chinese
AB HPLC is used to dets. the content of monacolin K in fermentation samples of Monascus sp. with methanol/0.18% phosphoric acid (77:23) as mobile phase at a flow rate of 0.6 mL/min and the detection wavelength of 237 nm. The content of Monacolin K is determined by external standard method. The relative standard deviation and average recovery are 0.27% and 98.92%, resp. Red-koji rice was extracted by methanol, and monacolin K was extracted by shaking for 2.5-3 h with the revolving rate of 200 r/min at 30℃. The filtrate of Monascus sp. was directly used to determine monacolin K, because the filtrate contained more than 50% monacolin K. The method is simple and effective, and can be used for the research work and quality control of functional products derived from Monascus sp.
IT 75330-75-5P, Monacolin K
RL: ANT (Analyte); BMF (Bioindustrial manufacture); ANST (Analytical study); BIOL (Biological study); PREP (Preparation)
(determination of monacolin K in fermentation of Monascus sp. by HPLC)
RN 75330-75-5 HCAPLUS
CN Butanoic acid, 2-methyl-, (1S,3R,7S,8S,8aR)-1,2,3,7,8,8a-hexahydro-3,7-dimethyl-8-[2-[(2R,4R)-tetrahydro-4-hydroxy-6-oxo-2H-pyran-2-yl]ethyl]-1-naphthalenyl ester, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



L91 ANSWER 17 OF 45 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:570510 HCAPLUS Full-text
DOCUMENT NUMBER: 141:128827
TITLE: Process for obtaining HMG-CoA reductase inhibitors of high purity
INVENTOR(S): Grahek, Rok; Milivojevic, Dusan; Bastarda, Andrej
PATENT ASSIGNEE(S): Lek Pharmaceuticals d.d., Slovenia
SOURCE: U.S. Pat. Appl. Publ., 12 pp., Cont.-in-part of U.S. 6,695,969.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

US 2004138294	A1	20040715	US 2003-698009		20031030
US 7141602	B2	20061128			
SI 20072	A	20000430	SI 1998-241		19980918
WO 2000017182	A1	20000330	WO 1999-IB1553		19990917
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW					
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG					
US 6695969	B1	20040224	US 2001-720952		20010103
US 2007032549	A1	20070208	US 2006-581637		20061016
PRIORITY APPLN. INFO.:			SI 1998-241	A	19980918
			WO 1999-IB1553	W	19990917
			US 2001-720952	A2	20010103
			US 2003-698009	A3	20031030

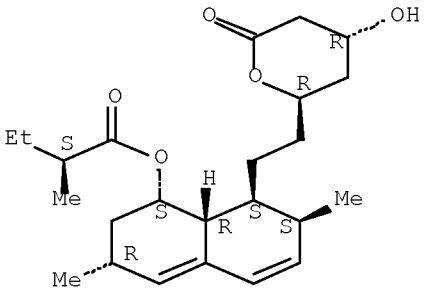
AB Lovastatin, pravastatin, simvastatin, mevastatin, atorvastatin, and derivs. and analogs thereof are known as HMG-CoA reductase inhibitors and are used as anticholesteremic agents. The majority of them are produced by fermentation by using microorganisms of different species identified as species belonging to Aspergillus, Monascus, Nocardia, Amycolatopsis, Mucor or Penicillium genus, Streptomyces, Actinomadura, Micromonospora, some are obtained by treating the fermentation products using the method of chemical synthesis or they are the products of total chemical synthesis. The purity of the active ingredient is an important factor for manufacturing the effective pharmaceutical, especially if the pharmaceutical product must be taken on a longer term basis in the treatment or prevention of high plasma cholesterol. The accumulation of the impurities from the pharmaceuticals of lower purity may cause many side effects during the medical treatment. The present invention relates to a new industrial process for the isolation of HMG-CoA reductase inhibitors using so-called displacement chromatog. Use of the invention enables one to obtain HMG-CoA reductase inhibitors of high purity, with high yields, and suitable ecol. balance. Crude sodium salt of pravastatin (1.0 g, purity 88%, assay 85%) was dissolved in 10 mL of the mobile phase A (distilled water), pH was adjusted to 7 with 0.2M aqueous NaOH solution and filtered. The column was equilibrated with mobile phase A. The sample obtained in the above-described manner was fed onto the Grom-Sil 120-ODS HE column, (column size 250×10 mm). The fractions with a purity of ≥99.5% were pooled and in the pooled fractions (7 mL) the HPLC purity was 99.8%.

IT 75330-75-5P, Lovastatin lactone
RL: PUR (Purification or recovery); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(process for obtaining HMG-CoA reductase inhibitors of high purity)

RN 75330-75-5 HCAPLUS

CN Butanoic acid, 2-methyl-, (1S,3R,7S,8S,8aR)-1,2,3,7,8,8a-hexahydro-3,7-dimethyl-8-[2-[(2R,4R)-tetrahydro-4-hydroxy-6-oxo-2H-pyran-2-yl]ethyl]-1-naphthalenyl ester, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



L91 ANSWER 18 OF 45 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:155656 HCAPLUS Full-text
DOCUMENT NUMBER: 140:205215
TITLE: Process for obtaining HMG-CoA reductase inhibitors of high purity
INVENTOR(S): Grahek, Rok; Milivojevic, Dusan; Bastarda, Andrej
PATENT ASSIGNEE(S): LEK Pharmaceuticals D.D., Slovenia
SOURCE: U.S., 6 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6695969	B1	20040224	US 2001-720952	20010103
SI 20072	A	20000430	SI 1998-241	19980918
WO 2000017182	A1	20000330	WO 1999-IB1553	19990917
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 2004138294	A1	20040715	US 2003-698009	20031030
US 7141602	B2	20061128		
US 2007032549	A1	20070208	US 2006-581637	20061016

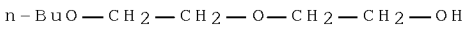
PRIORITY APPLN. INFO.:

SI 1998-241	A	19980918
WO 1999-IB1553	W	19990917
US 2001-720952	A2	20010103
US 2003-698009	A3	20031030

AB Lovastatin, pravastatin, simvastatin, mevastatin, atorvastatin, and derivs. and analogs thereof are known as HMG-CoA reductase inhibitors and are used as antihypercholesterolemic agents. The majority of them are produced by fermentation using microorganisms of different species identified as species belonging to Aspergilus, Monascus, Nocardia, Amycolatopsis, Mucor or Penicilium genus, some are obtained by treating the fermentation products using the method of chemical synthesis or they are the products of total chemical synthesis. The purity of the active ingredient is an important factor for manufacturing the safe and effective pharmaceutical, especially if the pharmaceutical product must be taken on a longer term basis in the

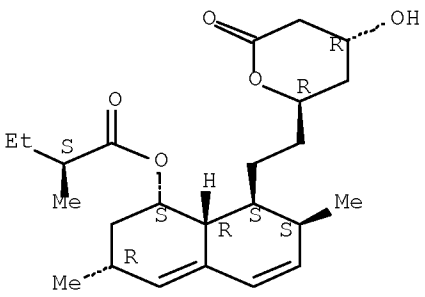
treatment or prevention of high plasma cholesterol. The accumulation of the impurities from the pharmaceuticals of lower purity may cause many side effects during the medical treatment. The present invention relates to a new industrial process for the isolation of HMG-CoA reductase inhibitors using so-called displacement chromatog. Use of the invention enables to obtain HMG-CoA reductase inhibitors of high purity, with high yields, lower production costs and suitable ecol. balance.

IT 112-34-5, Diethylene glycol monobutyl ether
RL: ARU (Analytical role, unclassified); ANST (Analytical study)
(column washed with mobile phase containing; displacement chromatog. for obtaining HMG-CoA reductase inhibitors of high purity)
RN 112-34-5 HCAPLUS
CN Ethanol, 2-(2-butoxyethoxy)- (CA INDEX NAME)



IT 75330-75-5P, Lovastatin lactone
RL: PUR (Purification or recovery); RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(displacement chromatog. for obtaining HMG-CoA reductase inhibitors of high purity)
RN 75330-75-5 HCAPLUS
CN Butanoic acid, 2-methyl-, (1S,3R,7S,8S,8aR)-1,2,3,7,8,8a-hexahydro-3,7-dimethyl-8-[2-[(2R,4R)-tetrahydro-4-hydroxy-6-oxo-2H-pyran-2-yl]ethyl]-1-naphthalenyl ester, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L91 ANSWER 19 OF 45 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:434162 HCAPLUS Full-text
DOCUMENT NUMBER: 139:6712
TITLE: Process for preparation of lovastatin and simvastatin by lactonization
INVENTOR(S): Lee, Kwang-hyeg; Kim, Jin-wan; Choi, Kwang-do; Lee, Sang-ho; Cho, Hong-suk
PATENT ASSIGNEE(S): CJ Corporation, S. Korea
SOURCE: Eur. Pat. Appl., 10 pp.

CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1316552	A1	20030604	EP 2002-26916	20021203
EP 1316552	B1	20060222		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
KR 2003045340	A	20030611	KR 2001-75991	20011203
WO 2003048149	A1	20030612	WO 2002-KR2095	20021111
W: AE, AG, AL, AM, AT, AZ, BA, BB, BG, BY, BZ, CH, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, KE, KG, KP, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2003109723	A1	20030612	US 2002-295300	20021114
US 6906204	B2	20050614		
CA 2413235	A1	20030603	CA 2002-2413235	20021129
CA 2413235	C	20060530		
CN 1425661	A	20030625	CN 2002-153037	20021129
AU 2002311322	A1	20030612	AU 2002-311322	20021202
JP 2003183271	A	20030703	JP 2002-350255	20021202
JP 3802481	B2	20060726		
BR 2002004943	A	20040615	BR 2002-4943	20021202
MX 2002PA11967	A	20040716	MX 2002-PA11967	20021202
AT 318264	T	20060315	AT 2002-26916	20021203
IN 2004CN01213	A	20060210	IN 2004-CN1213	20040602
PRIORITY APPLN. INFO.:			KR 2001-75991 A	20011203
			WO 2002-KR2095 W	20021111

OTHER SOURCE(S): CASREACT 139:6712; MARPAT 139:6712

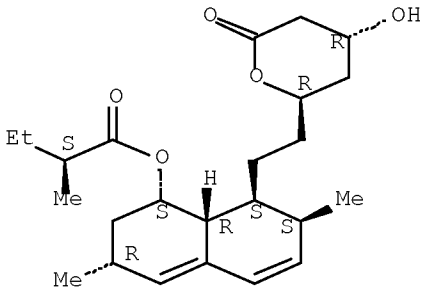
AB The present invention relates to a processing method for preparing lovastatin and simvastatin which comprises the steps of (1) performing lactonization of mevinic acid and its homologous compds. in the presence of a mixed organic solvent without an acid catalyst through nitrogen sweep; and (2) crystallization In the process lovastatin and simvastatin can be produced in a high yield with high purity and heterodimers formed as a byproduct can be reduced remarkably. Therefore, the processing method of the present invention can be convenient and economical.

IT 75330-75-5P, Lovastatin
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(process for preparation of lovastatin and simvastatin by lactonization)

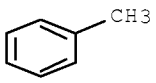
RN 75330-75-5 HCAPLUS

CN Butanoic acid, 2-methyl-, (1S,3R,7S,8S,8aR)-1,2,3,7,8,8a-hexahydro-3,7-dimethyl-8-[2-[(2R,4R)-tetrahydro-4-hydroxy-6-oxo-2H-pyran-2-yl]ethyl]-1-naphthalenyl ester, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



IT 108-88-3, Toluene, uses
RL: NUU (Other use, unclassified); USES (Uses)
(process for preparation of lovastatin and simvastatin by lactonization)
RN 108-88-3 HCAPLUS
CN Benzene, methyl- (CA INDEX NAME)



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L91 ANSWER 20 OF 45 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:172972 HCAPLUS Full-text
DOCUMENT NUMBER: 138:221390
TITLE: Process of lactonization and crystallization in the preparation of highly purified statins
INVENTOR(S): Lee, Kwang-Hyeg; Kim, Jin-Wan; Yoon, Myeong-Sik; Choi, Kwang-Do; Lee, Sang-Ho; Cho, Hong-Suk
PATENT ASSIGNEE(S): Cheil Jedang Corporation, S. Korea
SOURCE: Eur. Pat. Appl., 11 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

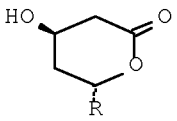
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1288212	A1	20030305	EP 2002-15509	20020710
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
KR 2003018202	A	20030306	KR 2001-51796	20010827
WO 2003018570	A1	20030306	WO 2002-KR1281	20020706
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, KE, KG, KP, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW				

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

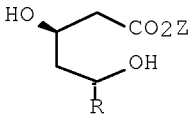
AU 2002315934	A1	20030310	AU 2002-315934		20020706
US 2003050482	A1	20030313	US 2002-200174		20020723
US 6649775	B2	20031118			
CN 1406938	A	20030402	CN 2002-127086		20020729
JP 2003096071	A	20030403	JP 2002-245931		20020826
PRIORITY APPLN. INFO.:			KR 2001-51796	A	20010827
			WO 2002-KR1281	W	20020706

OTHER SOURCE(S): CASREACT 138:221390; MARPAT 138:221390

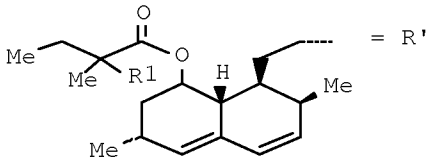
GI



I

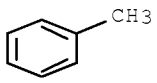


II



AB The present invention relates to a process for preparing lovastatin (I; R = R', R1 = α-H) and simvastatin (I; R = R', R1 = Me) which comprises a step of (1) performing a lactonization of mevinic acid analogs II (Z = H, NH4, metal cation) in the presence of a dehydrating agent and without an acid catalyst under nitrogen sweep; and then a step of (2) making crystals at a high temperature In the process of the present invention, I can be produced highly purified in a high yield and, especially, heterodimers formed as a byproduct can be reduced in an amount remarkably. Therefore, the process of the present invention is convenient and economical.

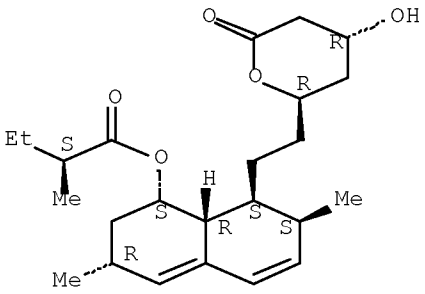
IT 108-88-3, Toluene, uses
RL: NUU (Other use, unclassified); USES (Uses)
(crystallization solvent or co-solvent; preparation of highly purified statins via lactonization of mevinic acid analogs and crystallization)
RN 108-88-3 HCAPLUS
CN Benzene, methyl- (CA INDEX NAME)



IT 75330-75-5P, Lovastatin

RL: PUR (Purification or recovery); SPN (Synthetic preparation); PREP (Preparation)
(preparation of highly purified statins via lactonization of mevinic acid analogs and crystallization)
RN 75330-75-5 HCAPLUS
CN Butanoic acid, 2-methyl-, (1S,3R,7S,8S,8aR)-1,2,3,7,8,8a-hexahydro-3,7-dimethyl-8-[2-[(2R,4R)-tetrahydro-4-hydroxy-6-oxo-2H-pyran-2-yl]ethyl]-1-naphthalenyl ester, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L91 ANSWER 21 OF 45 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:963759 HCAPLUS Full-text
DOCUMENT NUMBER: 138:38145
TITLE: Fermentation media for the production of pravastatin and lovastatin
INVENTOR(S): Benedetti, Alberto; Manzoni, Matilde; Nichele, Marina; Rollini, Manuela
PATENT ASSIGNEE(S): Gnosis Srl, Italy
SOURCE: Eur. Pat. Appl., 15 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1266967	A1	20021218	EP 2001-114462	20010615
EP 1266967	B1	20040128		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
AT 258603	T	20040215	AT 2001-114462	20010615
PT 1266967	T	20040531	PT 2001-114462	20010615
ES 2210066	T3	20040701	ES 2001-1114462	20010615

PRIORITY APPLN. INFO.: EP 2001-114462 A 20010615
AB A fermentation process is provided for the production of exocellular pravastatin which comprises cultivating microorganisms from Aspergillus terreus and Monascus ruber strains with suitable carbon, nitrogen and minerals in the culture medium. The process of the invention allows to obtain exocellular pravastatin, directly in a fermentation medium, with production yields well above 500 mg/l. Lovastatin is also produced from Aspergillus.

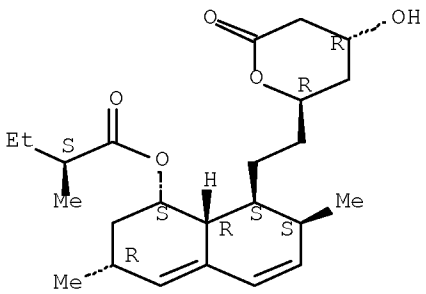
CThus Monascus ruber DSM 13554 was cultivated in a batch fermentation on a medium comprising 65 g/L glycerol, 30 g/L glucose, 10 g/L peptone, 25 g/L defatted soy flour, 2 g/L sodium nitrate, and 0.5 g/L magnesium sulfate. After 96 h cultivation at 25 ℃, 3065 mg/L of pravastatin was produced.

IT 75330-75-5P, Lovastatin
RL: BMF (Bioindustrial manufacture); PUR (Purification or recovery); BIOL (Biological study); PREP (Preparation)
(fermentation media for production of pravastatin and lovastatin)

RN 75330-75-5 HCAPLUS

CN Butanoic acid, 2-methyl-, (1S,3R,7S,8S,8aR)-1,2,3,7,8,8a-hexahydro-3,7-dimethyl-8-[2-[(2R,4R)-tetrahydro-4-hydroxy-6-oxo-2H-pyran-2-yl]ethyl]-1-naphthalenyl ester, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L91 ANSWER 22 OF 45 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:76963 HCAPLUS Full-text
DOCUMENT NUMBER: 136:117427
TITLE: Extraction of monacolin K from red koji
INVENTOR(S): Kadoya, Isao; Tanabe, Nobukazu; Nishimura, Minoru
PATENT ASSIGNEE(S): Gunze, Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 3 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2002027996	A	20020129	JP 2000-212079	20000713

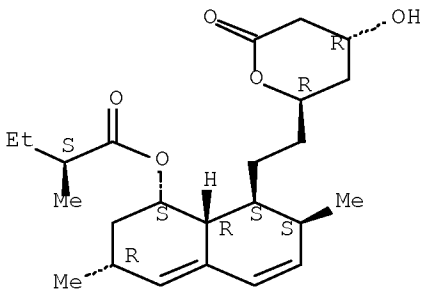
PRIORITY APPLN. INFO.: JP 2000-212079 20000713

AB Monacolin K (I) is extracted with 40-80 volume/volume% aqueous EtOH solution from red koji manufactured by cultivation of Monascus sp. Thus, rice was soaked in water, drained, mixed with powdered rice germ, inoculated with M. pilosus IFO 4520, still cultured, the enzyme deactivated, and extracted with 50% or 60% aqueous EtOH solution to extract 79 μg I/mL.

IT 75330-75-5P, Monacolin K
RL: BMF (Bioindustrial manufacture); PEP (Physical, engineering or chemical process); PUR (Purification or recovery); PYP (Physical process); BIOL (Biological study); PREP (Preparation); PROC

(Process)
(extraction of monacolin K from red koji with aqueous EtOH)
RN 75330-75-5 HCAPLUS
CN Butanoic acid, 2-methyl-, (1S,3R,7S,8S,8aR)-1,2,3,7,8,8a-hexahydro-3,7-dimethyl-8-[2-[(2R,4R)-tetrahydro-4-hydroxy-6-oxo-2H-pyran-2-yl]ethyl]-1-naphthalenyl ester, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



L91 ANSWER 23 OF 45 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:676761 HCAPLUS Full-text
DOCUMENT NUMBER: 135:215976
TITLE: A process for purifying lovastatin and simvastatin with reduced levels of dimeric impurities
INVENTOR(S): Keri, Vilmos; Forgas, Ilona
PATENT ASSIGNEE(S): Biogal Gyogyszergyar Rt., Hung.; Teva Pharmaceuticals USA, Inc.
SOURCE: PCT Int. Appl., 17 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001066538	A1	20010913	WO 2001-US6334	20010227
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2402061	A1	20010913	CA 2001-2402061	20010227
US 2002002288	A1	20020103	US 2001-793946	20010227
US 6521762	B2	20030218		
EP 1265884	A1	20021218	EP 2001-913139	20010227
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
HU 2003001214	A2	20030828	HU 2003-1214	20010227
JP 2003525935	T	20030902	JP 2001-565354	20010227

TR 200403001	T3	20050221	TR 2004-3001		20010227
ZA 2002007023	A	20030902	ZA 2002-7023		20020902
PRIORITY APPLN. INFO.:			US 2000-186868P	P	20000303
			WO 2001-US6334	W	20010227

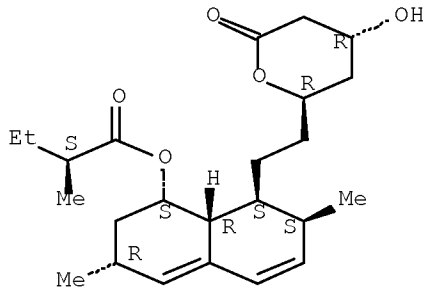
AB Disclosed is a process for reducing the levels of dimeric impurities in a statin to less than 0.08 % by treatment of a statin containing more than 0.08 % dimeric impurities with a mild base in a suitable solvent mixture Lovastatin (in its lactone forms) was dissolved in a mixture of iso-Bu acetate and ethanol (3:1). This mixture was heated at 40-70° and concentrated NH4OH solution was added to the solution The mixture was cooled to give a product containing lovastatin dimer at ≤ 0.08 %.

IT 75330-75-5P, Lovastatin
RL: PUR (Purification or recovery); PREP (Preparation)
(mild base in alc. solvents for purifying lovastatin and simvastatin with reduced levels of dimeric impurities)

RN 75330-75-5 HCAPLUS

CN Butanoic acid, 2-methyl-, (1S,3R,7S,8S,8aR)-1,2,3,7,8,8a-hexahydro-3,7-dimethyl-8-[2-[(2R,4R)-tetrahydro-4-hydroxy-6-oxo-2H-pyran-2-yl]ethyl]-1-naphthalenyl ester, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L91 ANSWER 24 OF 45 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER:	2001:636241 HCAPLUS Full-text
DOCUMENT NUMBER:	135:194535
TITLE:	Method of purifying a fermentation broth
INVENTOR(S):	Keri, Vilmos; Deak, Lajos; Forgacs, Ilona
PATENT ASSIGNEE(S):	Biogal Gyogyszergyar Rt, Hung.; Teva Pharmaceuticals USA Inc.
SOURCE:	PCT Int. Appl., 22 pp. CODEN: PIXXD2
DOCUMENT TYPE:	Patent
LANGUAGE:	English
FAMILY ACC. NUM. COUNT:	1
PATENT INFORMATION:	

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001062949	A1	20010830	WO 2001-US2505	20010125
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR,				

HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT,
LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU,
SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN,
YU, ZA, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

CA 2400952	A1	20010830	CA 2001-2400952		20010125
US 6387258	B1	20020514	US 2001-769684		20010125
EP 1263979	A1	20021211	EP 2001-908701		20010125
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR					
HU 2003000073	A2	20030528	HU 2003-73		20010125
JP 2003523751	T	20030812	JP 2001-561759		20010125
JP 3740062	B2	20060125			
RU 2265665	C2	20051210	RU 2002-122746		20010125
ZA 2002006496	A	20030923	ZA 2002-6496		20020814
IN 2002MN01116	A	20040605	IN 2002-MN1116		20020820
PRIORITY APPLN. INFO.:			US 2000-184522P	P	20000224
			WO 2001-US2505	W	20010125

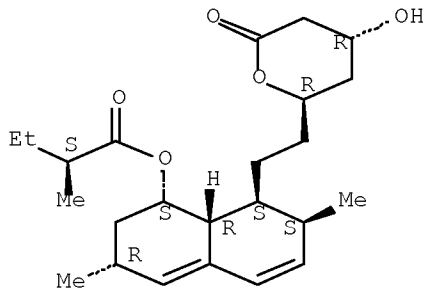
AB A process for purifying statin compds. from a fermentation broth by extraction and crystallization is disclosed. A fermentation broth is subjected to a pretreatment procedure which involves an alkaline pretreatment and an alkaline purification Following the pretreatment procedure, the statin compound is extracted under acidic conditions into a hydrophobic solvent and purified by crystallization The organic extraction solvent is concentrated and then extracted with a mild base. The statin compound is then purified by crystallization

IT 75330-75-5P, Lovastatin
RL: BMF (Bioindustrial manufacture); PUR (Purification or recovery); BIOL (Biological study); PREP (Preparation)
(purifying statins from a fermentation broth)

RN 75330-75-5 HCAPLUS

CN Butanoic acid, 2-methyl-, (1S,3R,7S,8S,8aR)-1,2,3,7,8,8a-hexahydro-3,7-dimethyl-8-[2-[(2R,4R)-tetrahydro-4-hydroxy-6-oxo-2H-pyran-2-yl]ethyl]-1-naphthalenyl ester, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L91 ANSWER 25 OF 45 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:416764 HCAPLUS Full-text
DOCUMENT NUMBER: 135:18608

TITLE: Process for recovering statin compounds from a fermentation broth
INVENTOR(S): Keri, Vilmos; Deak, Lajos; Forgacs, Ilona; Szabo, Csaba; Nagyne, Edit Arvai
PATENT ASSIGNEE(S): Biogal Gyogyszergyar Rt, Hung.; Teva Pharmaceuticals Usa, Inc.
SOURCE: PCT Int. Appl., 28 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001039768	A1	20010607	WO 2000-US32391	20001128
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2393057	A1	20010607	CA 2000-2393057	20001128
AU 200118046	A	20010612	AU 2001-18046	20001128
US 6444452	B1	20020903	US 2000-723711	20001128
EP 1265604	A1	20021218	EP 2000-980834	20001128
EP 1265604	B1	20061018		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
HU 2002004012	A2	20030328	HU 2002-4012	20001128
JP 2003515334	T	20030507	JP 2001-541501	20001128
JP 3881240	B2	20070214		
EP 1481674	A1	20041201	EP 2004-10770	20001128
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, CY, TR				
CN 1754872	A	20060405	CN 2005-10073912	20001128
AT 342717	T	20061115	AT 2000-980834	20001128
ES 2273737	T3	20070516	ES 2000-980834	20001128
EP 1798214	A2	20070620	EP 2007-1703	20001128
EP 1798214	A3	20070801		
R: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE, TR, SI				
ZA 2002003912	A	20030821	ZA 2002-3912	20020516
MX 2002PA05283	A	20031006	MX 2002-PA5283	20020528
US 2002187531	A1	20021212	US 2002-200149	20020723
US 6689590	B2	20040210		
US 2004115781	A1	20040617	US 2003-700567	20031105
JP 2004350687	A	20041216	JP 2004-206262	20040713
JP 2006055174	A	20060302	JP 2005-304900	20051019
JP 2006273861	A	20061012	JP 2006-141646	20060522

PRIORITY APPLN. INFO.:		
US 1999-168056P	P	19991130
CN 2000-818725	A3	20001128
EP 2000-980834	A3	20001128
EP 2004-10770	A3	20001128
JP 2001-541501	A3	20001128

US 2000-723711	A1	20001128
WO 2000-US32391	W	20001128
US 2002-200149	A1	20020723
JP 2004-206262	A3	20040713

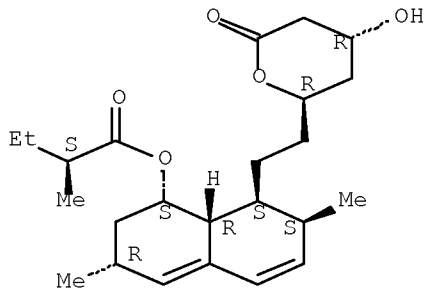
AB A novel process for recovering a compound from a fermentation broth that includes the stages of forming an enriched solution of the compound by extraction, obtaining a salt of the compound from the enriched solution, purifying a salt of the compound and exchanging the salt of the compound to a metal salt of the compound is disclosed. Thus, pravastatin was extracted by iso-Bu acetate from fermentation broth which had been acidified to pH 2.5 by sulfuric acid. The the pH of the solvent extract was then adjusted to 11 by the addition of aqueous ammonium hydroxide and the resulting aqueous pravastatin solution was re-acidified and then back extracted with iso-Bu acetate. After the iso-Bu acetate extract had been partially dried and decolorized with activated charcoal, ammonia gas was added to the headspace of the solution until all precipitation ceased. The precipitated ammonium pravastatin salt was collected by filtration, washed with solvents, diluted in water, acetone and iso-Bu acetate, crystallized by the addition of solid ammonium chloride. The crystallized ammonium pravastatin further crystallized in isobutanol. The ammonium pravastatin salt crystals were then dissolved in a water and iso-Bu acetate was added. The solution was acidified to ph 2-4 with sulfuric acid, washed with water and the pravastatin was converted to its sodium salt by the intermittent addition of sodium hydroxide. Excess sodium ions were removed by ion exchange and the sodium pravastatin salt was crystallized in a water/acetonitrile/acetone solvent. A sodium pravastatin yield of 65% with a purity of 99.3% was obtained with this process.

IT 75330-75-5P, Lovastatin
RL: BMF (Bioindustrial manufacture); BPN (Biosynthetic preparation); PUR (Purification or recovery); BIOL (Biological study); PREP (Preparation)
(process for recovering statin compds. from a fermentation broth)

RN 75330-75-5 HCAPLUS

CN Butanoic acid, 2-methyl-, (1S,3R,7S,8S,8aR)-1,2,3,7,8,8a-hexahydro-3,7-dimethyl-8-[2-[(2R,4R)-tetrahydro-4-hydroxy-6-oxo-2H-pyran-2-yl]ethyl]-1-naphthalenyl ester, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



IT 7647-01-0, Hydrochloric acid, reactions
RL: RCT (Reactant); RACT (Reactant or reagent)
(process for recovering statin compds. from a fermentation broth)

RN 7647-01-0 HCAPLUS

CN Hydrochloric acid (CA INDEX NAME)

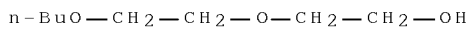
HCl

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L91 ANSWER 26 OF 45 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:334067 HCAPLUS Full-text
DOCUMENT NUMBER: 135:225890
TITLE: Chromatographic purification of some 3-hydroxy-3-methylglutaryl coenzyme A reductase inhibitors
AUTHOR(S): Grahek, R.; Milivojevic, D.; Bastarda, A.; Kracun, M.
CORPORATE SOURCE: Research and Development, Lek d.d., Ljubljana, 1526, Slovenia
SOURCE: Journal of Chromatography, A (2001), 918(2), 319-324
CODEN: JCRAEY; ISSN: 0021-9673
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

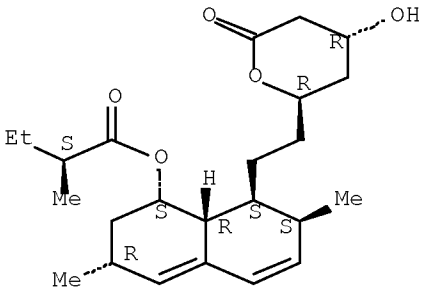
AB The purification of pravastatin, simvastatin and lovastatin in the sodium salt or lactone form and of mevastatin in the lactone form by reversed-phase displacement chromatog. is presented. The mobile phases consisted of water or mixts. of water-methanol and water-acetonitrile. Six different displacers were successfully used. Up to 0.14 g of raw sample per g of stationary phase was loaded on a column packed with silica-based octadecyl phase. Crude substances from 85 to 88% chromatog. purity were purified and at least 99.5% purity was achieved.

IT 112-34-5, Diethyleneglycol monobutyl ether
RL: NUU (Other use, unclassified); USES (Uses)
(chromatog. purification of 3-hydroxy-3-methylglutaryl CoA reductase inhibitors)
RN 112-34-5 HCAPLUS
CN Ethanol, 2-(2-butoxyethoxy)- (CA INDEX NAME)



IT 75330-75-5P
RL: PUR (Purification or recovery); PREP (Preparation)
(chromatog. purification of 3-hydroxy-3-methylglutaryl CoA reductase inhibitors)
RN 75330-75-5 HCAPLUS
CN Butanoic acid, 2-methyl-, (1S,3R,7S,8S,8aR)-1,2,3,7,8,8a-hexahydro-3,7-dimethyl-8-[2-[(2R,4R)-tetrahydro-4-hydroxy-6-oxo-2H-pyran-2-yl]ethyl]-1-naphthalenyl ester, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L91 ANSWER 27 OF 45 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:319886 HCAPLUS Full-text
DOCUMENT NUMBER: 134:328208
TITLE: Lactonization process for preparation of 3-hydroxylactone-containing products
INVENTOR(S): McManus, James; Anousis, Nicholas; Genus, John; Hancock, Christopher
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 31 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001030773	A2	20010503	WO 2000-US29220	20001023
WO 2001030773	A3	20010614		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2388182	A1	20010503	CA 2000-2388182	20001023
US 6380401	B1	20020430	US 2000-694190	20001023
EP 1228057	A2	20020807	EP 2000-971010	20001023
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
US 2002156298	A1	20021024	US 2002-117580	20020405
US 6525205	B2	20030225		

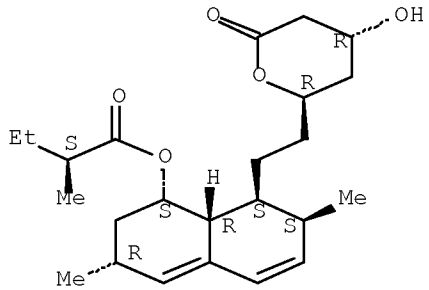
PRIORITY APPLN. INFO.:	US 1999-161876P	P	19991027
	US 2000-694190	A3	20001023
	WO 2000-US29220	W	20001023

OTHER SOURCE(S): MARPAT 134:328208
AB Crystalline 3-hydroxylactone-containing products can be prepared in high yield and purity in a one-pot process by treating the corresponding 3,5-dihydroxy acid with a strong mineral acid in a cold, aprotic, and water-miscible solvent

to effect lactonization, followed by addition of excess acid to effect crystallization of the lactonized product from the reaction mixture The process is useful in making 3-hydroxy-3-methylglutaryl CoA reductase inhibitors, such as simvatatin.

IT 75330-75-5P, Lovastatin
RL: IMF (Industrial manufacture); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(lactonization process for preparation of 3-hydroxylactone-containing products)
RN 75330-75-5 HCAPLUS
CN Butanoic acid, 2-methyl-, (1S,3R,7S,8S,8aR)-1,2,3,7,8,8a-hexahydro-3,7-dimethyl-8-[2-[(2R,4R)-tetrahydro-4-hydroxy-6-oxo-2H-pyran-2-yl]ethyl]-1-naphthalenyl ester, (2S)- (CA INDEX NAME)

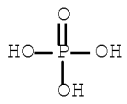
Absolute stereochemistry.



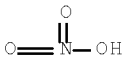
IT 7647-01-0, Hydrochloric acid, reactions
7664-38-2, Phosphoric acid, reactions 7697-37-2, Nitric acid, reactions
RL: RCT (Reactant); RACT (Reactant or reagent)
(lactonization process for preparation of 3-hydroxylactone-containing products)
RN 7647-01-0 HCAPLUS
CN Hydrochloric acid (CA INDEX NAME)

HCl

RN 7664-38-2 HCAPLUS
CN Phosphoric acid (CA INDEX NAME)



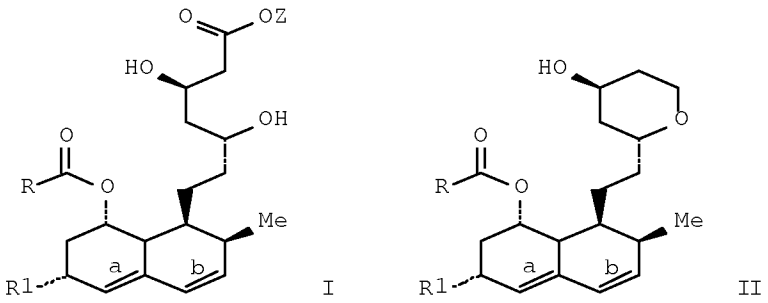
RN 7697-37-2 HCAPLUS
CN Nitric acid (CA INDEX NAME)



L91 ANSWER 28 OF 45 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:12440 HCAPLUS Full-text
DOCUMENT NUMBER: 134:71492
TITLE: Process for selective lactonization
INVENTOR(S): Fukae, Masafumi; Ueda, Makoto; Tatsuki, Kenichi
PATENT ASSIGNEE(S): Kaneka Corporation, Japan
SOURCE: PCT Int. Appl., 21 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2001000606	A1	20010104	WO 2000-JP4269		20000629
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM					
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG					
CA 2342361	A1	20010104	CA 2000-2342361		20000629
EP 1110959	A1	20010627	EP 2000-942379		20000629
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, MC, IE, SI, LT, LV, FI, RO					
SI 20527	A	20011031	SI 2000-20009		20000629
PRIORITY APPLN. INFO.:			JP 1999-183640	A	19990629
			WO 2000-JP4269	W	20000629

OTHER SOURCE(S): CASREACT 134:71492; MARPAT 134:71492
GI



I II

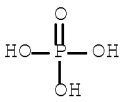
AB Described is a process for the lactonization of compds. of general formula (I; R = C1-10 alkyl; R1 = Me, CH2OH, CH2OCOR2, CO2R3, CONR4R5, OH, CH2OR2, CH2NR4R5; Z = H, NH4+, metal cation; R2 = C1-5 alkyl; R3 = H, C1-5 alkyl; R4 , R5 = H, C1-5 alkyl; both a and b bonds are a double; or one of a nd b bonds is single bond; or both an and b are a single bond) which makes it possible to suppress the formation of dimmers difficult to remove by conventional crystallization purification Specifically, a compound of general formula (II; R, R1, a, b = same as above) having a dimmer content of 0.3 mol % or below is prepared by lactonizing the corresponding compound of general formula I under such conditions that the solubility of the compound I and/or the compound II is 0.5 weight/weight% or below. Thus, aqueous solution of (3R,5R)-7-[(1S,2S,6R,8S,8aR)-1,2,6,7,8,8a-hexahydro-2,6-dimethyl-8-(2-methylbutyryloxy)-1-naphthyl]-3,5-dihydroxyheptanoic acid (4.0 weight%, 85 mL) was adjusted to pH 3 with H2SO4 and stirred at 70° for 6 h to give the lactone II (R = sec-Bu, R1 = Me; both a and b bond represent a double bond; Z = H) in 78%. The dimer content was 0.11 mL%.

IT 7647-01-0, Hydrochloric acid, uses
7664-38-2, Phosphoric acid, uses
RL: CAT (Catalyst use); USES (Uses)
(process for selective lactonization of [dimethyl(methylbutyryloxy)hexa hydronaphthyl]dihydroxyheptanoic acid derivative to (hexahydronaphthylethyl)hydroxytetrahydropyranone derivative in alkane or alkene)

RN 7647-01-0 HCAPLUS
CN Hydrochloric acid (CA INDEX NAME)

HCl

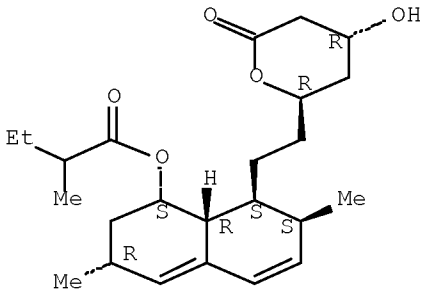
RN 7664-38-2 HCAPLUS
CN Phosphoric acid (CA INDEX NAME)



IT 237073-61-9P
RL: SPN (Synthetic preparation); PREP (Preparation)
(process for selective lactonization of [dimethyl(methylbutyryloxy)hexa hydronaphthyl]dihydroxyheptanoic acid derivative to (hexahydronaphthylethyl)hydroxytetrahydropyranone derivative in alkane or alkene)

RN 237073-61-9 HCAPLUS
CN Butanoic acid, 2-methyl-, (1S,3R,7S,8S,8aR)-1,2,3,7,8,8a-hexahydro-3,7-dimethyl-8-[2-[(2R,4R)-tetrahydro-4-hydroxy-6-oxo-2H-pyran-2-yl]ethyl]-1-naphthalenyl ester (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L91 ANSWER 29 OF 45 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2000:756893 HCAPLUS Full-text
DOCUMENT NUMBER: 133:309069
TITLE: Process for isolation of lovastatin from fermentation broth
INVENTOR(S): Jakubcova, Mari; Bosansky, Milos; Lucina, Dusan; Borosova, Gabriela
PATENT ASSIGNEE(S): Biotika A.S., Slovakia
SOURCE: PCT Int. Appl., 12 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

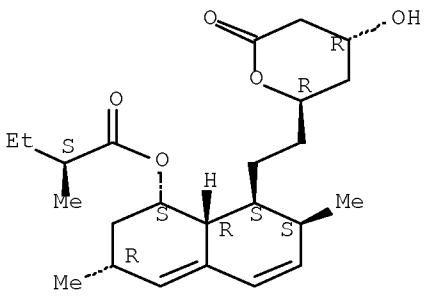
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000063411	A1	20001026	WO 2000-SK4	20000327
W: CZ, TR				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
SK 282679	B6	20021106	SK 1999-513	19990416
PRIORITY APPLN. INFO.:			SK 1999-513 A	19990416

AB A process of isolation of lovastatin aimed at obtaining a product that complies with the pharmacopoeial criteria is described. The process consists of the extraction of lovastatin from Aspergillus terreus fermentation broth at an alkaline pH value. In this process, the fermentation broth is adjusted to pH 10.0-11.0 with a suitable base, held for a determined time, the biomass is separated, and the filtrate containing lovastatin is extracted directly into an organic phase consisting of carboxylic acid esters and alkanes in the presence of a cation-active or a non-ionic demulsifier in an acidic pH range. The rich organic extract of lovastatin obtained by using this process has high purity and no purification by chromatog. is needed. The lovastatin rich organic extract is subjected to vacuum distillation at a temperature above 40 > ℃ in the presence of acetic acid where the resulting lactone is concentrated Crystallization takes place under cooling at 5 > ℃. The obtained crude product is recrystd. at an elevated temperature

IT 75330-75-5P, Lovastatin
RL: BMF (Bioindustrial manufacture); BPN (Biosynthetic preparation); PUR (Purification or recovery); BIOL (Biological study); PREP (Preparation)

(isolation of lovastatin from fermentation broth)
RN 75330-75-5 HCAPLUS
CN Butanoic acid, 2-methyl-, (1S,3R,7S,8S,8aR)-1,2,3,7,8,8a-hexahydro-3,7-dimethyl-8-[2-[(2R,4R)-tetrahydro-4-hydroxy-6-oxo-2H-pyran-2-yl]ethyl]-1-naphthalenyl ester, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L91 ANSWER 30 OF 45 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1999:549397 HCAPLUS Full-text
DOCUMENT NUMBER: 131:156982
TITLE: Process for the obtaining of HMG-CoA reductase inhibitors of high purity
INVENTOR(S): Pflaum, Zlatko; Milivojevic, Dusan; Senica, David
PATENT ASSIGNEE(S): Lek Pharmaceutical and Chemical Company D.D., Slovenia
SOURCE: PCT Int. Appl., 28 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9942601	A1	19990826	WO 1999-IB808	19990217
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2321052	A1	19990826	CA 1999-2321052	19990217
AU 9934384	A	19990906	AU 1999-34384	19990217
AU 743619	B2	20020131		
EP 1054993	A1	20001129	EP 1999-915976	19990217
EP 1054993	B1	20050525		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
HU 2001000820	A2	20010828	HU 2001-820	19990217
JP 2002504345	T	20020212	JP 2000-532541	19990217

RU 2235130	C2	20040827	RU 2000-124064	19990217
AT 296357	T	20050615	AT 1999-915976	19990217
SK 285074	B6	20060504	SK 2000-1185	19990217
CZ 297093	B6	20060913	CZ 2000-2856	19990217
RO 120922	B1	20060929	RO 2000-828	19990217
PL 193510	B1	20070228	PL 1913-3425	19990217
HR 2000000541	A1	20011231	HR 2000-541	20000816
BG 104696	A	20010731	BG 2000-104696	20000817
BG 64289	B1	20040831		
US 6825015	B1	20041130	US 2000-600566	20001016
JP 2005110693	A	20050428	JP 2004-372018	20041222

PRIORITY APPLN. INFO.:

SI 1998-46	A	19980218
JP 2000-532541	A3	19990217
WO 1999-IB808	W	19990217

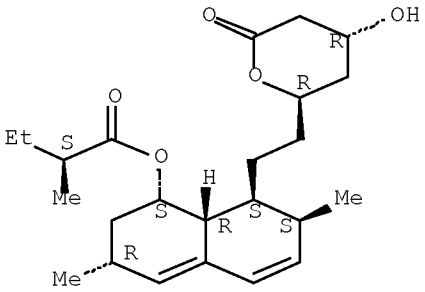
AB A process for the isolation and purification of HMG-CoA reductase inhibitors from a mycelium biomass is described, which process comprises: clarifying a mycelium broth and concentrating the clarified broth to a lower volume, acidifying of the concentrate to a pH value in the range of 4.5 to 7.5, followed by extracting the HMG-CoA reductase inhibitor with Et acetate, crystallization of the HMG-CoA reductase inhibitor from a water-miscible or water-soluble organic solvent, and crystallization of the HMG-CoA reductase inhibitor from an organic solvent having limited miscibility or solubility with water. The crystallization steps may also be reverse. The concept of a combination of the specified crystallization steps can also be used for the purification of a crude HMG-CoA reductase inhibitor.

IT 75330-75-5P, Lovastatin
RL: PUR (Purification or recovery); PREP (Preparation)
(process for obtaining of HMG-CoA reductase inhibitors of high purity)

RN 75330-75-5 HCAPLUS

CN Butanoic acid, 2-methyl-, (1S,3R,7S,8S,8aR)-1,2,3,7,8,8a-hexahydro-3,7-dimethyl-8-[2-[(2R,4R)-tetrahydro-4-hydroxy-6-oxo-2H-pyran-2-yl]ethyl]-1-naphthalenyl ester, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L91 ANSWER 31 OF 45 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1999:518314 HCAPLUS Full-text
DOCUMENT NUMBER: 131:157706
TITLE: Process of lactonization in the preparation of statins
INVENTOR(S): Kumar, Yatendra; Thaper, Rajesh Kumar; Kumar, S. M. Dileep; Khanna, Jag Mohan
PATENT ASSIGNEE(S): Ranbaxy Laboratories Limited, India

SOURCE: U.S., 4 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5939564	A	19990817	US 1998-55572	19980406
PRIORITY APPLN. INFO.:			IN 1997-3101 A	19971028

OTHER SOURCE(S): CASREACT 131:157706

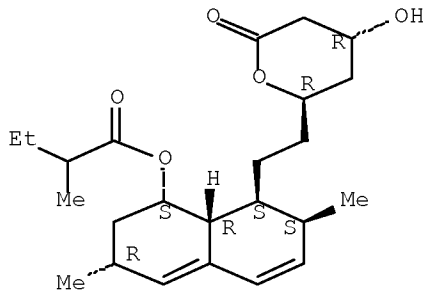
AB The title process comprises treating the open ring hydroxy-acid form of the statins or a salt thereof in an organic solvent by heating under anhydrous conditions in the presence of a catalyst comprising a salt of an organic base with an organic or inorg. acid such as pyridine hydrobromide.

IT 237073-61-9P
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(process of lactonization in the preparation of statins)

RN 237073-61-9 HCAPLUS

CN Butanoic acid, 2-methyl-, (1S,3R,7S,8S,8aR)-1,2,3,7,8,8a-hexahydro-3,7-dimethyl-8-[2-[(2R,4R)-tetrahydro-4-hydroxy-6-oxo-2H-pyran-2-yl]ethyl]-1-naphthalenyl ester (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L91 ANSWER 32 OF 45 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1999:417399 HCAPLUS Full-text
DOCUMENT NUMBER: 131:58747
TITLE: Process of lactonization in the preparation of statins
PATENT ASSIGNEE(S): Ranbaxy Laboratories Limited, India
SOURCE: U.S., 4 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5917058	A	19990629	US 1998-64285	19980422

IN 186880	A1	20011201	IN 1997-DE3102	19971028
ZA 9810764	A	19990813	ZA 1998-10764	19981125
EP 955297	A1	19991110	EP 1998-123252	19981207
EP 955297	B1	20040421		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
AT 264849	T	20040515	AT 1998-123252	19981207
PT 955297	T	20040831	PT 1998-123252	19981207
ES 2217485	T3	20041101	ES 1998-123252	19981207
RU 2214407	C2	20031020	RU 1998-122366	19981209
HU 9802936	A2	19991129	HU 1998-2936	19981216
HK 1023572	A1	20050225	HK 2000-102749	20000508
PRIORITY APPLN. INFO.:			IN 1997-DE3102 A	19971028
			US 1998-64285 A	19980422

OTHER SOURCE(S): CASREACT 131:58747; MARPAT 131:58747

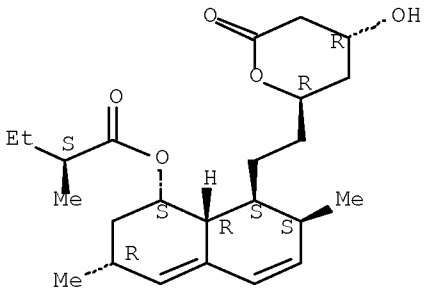
AB An improved process of lactonization in the preparation of statins (e.g., the HMG-CoA reductase inhibitors lovastatin and simvastatin) employs very mild reaction conditions. The improved process comprises treating the open ring hydroxy acid form of the statins with an excess of acetic acid and in the absence of a strong acid catalyst under mild heating conditions (e.g., ambient to 55° C.), and adding an anti-solvent to the reaction mixture, thereby causing the statins in lactone form to crystallize from the reaction mixture The acetic acid serves as both a solvent and a catalyst for the lactonization reaction.

IT 75330-75-5P
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(lactonization process in the preparation of statins)

RN 75330-75-5 HCAPLUS

CN Butanoic acid, 2-methyl-, (1S,3R,7S,8S,8aR)-1,2,3,7,8,8a-hexahydro-3,7-dimethyl-8-[2-[(2R,4R)-tetrahydro-4-hydroxy-6-oxo-2H-pyran-2-yl]ethyl]-1-naphthalenyl ester, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L91 ANSWER 33 OF 45 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1999:287867 HCAPLUS Full-text
DOCUMENT NUMBER: 131:43626
TITLE: Production of statins by filamentous fungi
AUTHOR(S): Manzoni, Matilde; Bergomi, Silvia; Rollini, Manuela; Cavazzoni, Valeria

CORPORATE SOURCE: Dipartimento di Scienze e Tecnologie Alimentari e Microbiologiche, Sezione di Microbiologia Industria, Universita degli Studi, Milan, 20133, Italy
SOURCE: Biotechnology Letters (1999), 21(3), 253-257
CODEN: BILED3; ISSN: 0141-5492
PUBLISHER: Kluwer Academic Publishers
DOCUMENT TYPE: Journal
LANGUAGE: English

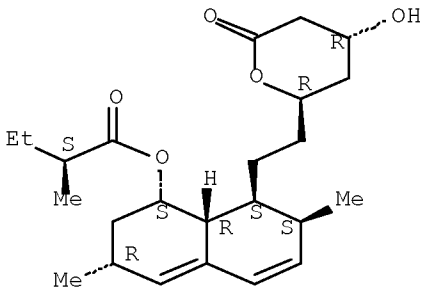
AB Several Monascus and Aspergillus strains were screened for statins production Lovastatin, monacolin J, pravastatin and mevastatin were produced, with higher yields from the A. terreus strains than from Monascus species. Of all the strains investigated M. paxii AM12M, an isolated spontaneous mutant, yielded 127 mg lovastatin/l and 53 mg pravastatin/l at 21 days, and 18 mg pravastatin/l at 16 days employing a whole soybean flour medium; A. terreus BST yielded 230 mg lovastatin/l and 118 mg pravastatin/l at 14 days employing a defatted soybean flour medium. Statins recovery showed that pravastatin was, in both strains, mostly found in both the mycelium and the culture filtrate, while lovastatin remained closely associated (83%) to the A. terreus mycelium or was mainly released into the culture filtrate (64%) of M. paxii culture.

IT 75330-75-5P, Lovastatin
RL: BMF (Bioindustrial manufacture); BIOL (Biological study); PREP (Preparation)
(production of statins by filamentous fungi)

RN 75330-75-5 HCAPLUS

CN Butanoic acid, 2-methyl-, (1S,3R,7S,8S,8aR)-1,2,3,7,8,8a-hexahydro-3,7-dimethyl-8-[2-[(2R,4R)-tetrahydro-4-hydroxy-6-oxo-2H-pyran-2-yl]ethyl]-1-naphthalenyl ester, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



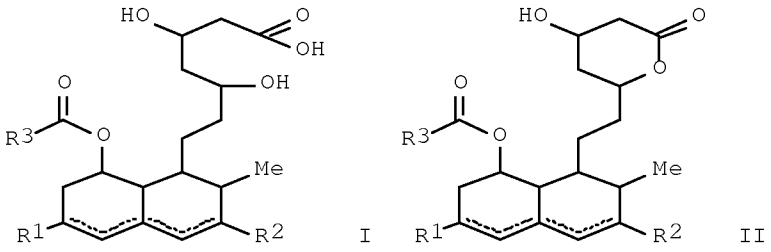
REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L91 ANSWER 34 OF 45 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1998:742217 HCAPLUS Full-text
DOCUMENT NUMBER: 129:342750
TITLE: HMG-CoA reductase inhibitor preparation process
PATENT ASSIGNEE(S): Gist-Brocades B.V., Neth.
SOURCE: Eur. Pat. Appl., 15 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 877089	A1	19981111	EP 1997-303111	19970507
R: NL				
WO 9850572	A1	19981112	WO 1998-EP2616	19980504
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9877613	A	19981127	AU 1998-77613	19980504
EP 980437	A1	20000223	EP 1998-925525	19980504
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
HU 2000002103	A2	20001028	HU 2000-2103	19980504
HU 2000002103	A3	20011029		
JP 2002510197	T	20020402	JP 1998-547725	19980504
US 6268186	B1	20010731	US 2000-423370	20000112
PRIORITY APPLN. INFO.:			EP 1997-303111 A	19970507
			WO 1998-EP2616 W	19980504

OTHER SOURCE(S): MARPAT 129:342750

GI



I II

AB A process for preparing a compound which is hydroxymethyl glutaryl CoA (HMG-CoA) reductase inhibitor (such as lovastatin, compactin, or pravastatin), or a precursor thereof (I or II: R1, R2 = H, Me, etc.; R3 = straight/branched C2-6 alkyl group), is disclosed where a broth containing the inhibitor (or its precursor) resulting from fermentation is basified prior to filtration to remove the biomass. The resulting filtrate is contacted with an adsorbent resin, acidified and the compound extracted using toluene, in which it is subsequently lactonized to give the inhibitor. The toluene containing the compound is then washed twice, firstly with alkaline, and then secondly with acidified, water, before being isolated by crystallization

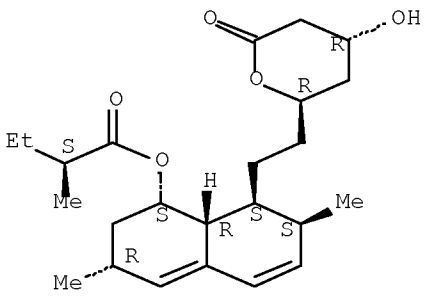
IT 75330-75-5P, Lovastatin
RL: BPN (Biosynthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(HMG-CoA reductase inhibitor preparation process)

RN 75330-75-5 HCAPLUS

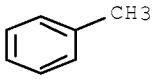
CN Butanoic acid, 2-methyl-, (1S,3R,7S,8S,8aR)-1,2,3,7,8,8a-hexahydro-3,7-dimethyl-8-[2-[(2R,4R)-tetrahydro-4-hydroxy-6-oxo-2H-pyran-2-yl]ethyl]-1-

naphthalenyl ester, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



IT 108-88-3, Toluene, uses
RL: NUU (Other use, unclassified); USES (Uses)
(HMG-CoA reductase inhibitor preparation process)
RN 108-88-3 HCAPLUS
CN Benzene, methyl- (CA INDEX NAME)



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L91 ANSWER 35 OF 45 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1998:539482 HCAPLUS Full-text
DOCUMENT NUMBER: 129:244177
TITLE: Production and purification of statins from Aspergillus terreus strains
AUTHOR(S): Manzoni, Matilde; Rollini, Manuela; Bergomi, Silvia; Cavazzoni, Valeria
CORPORATE SOURCE: Dipartimento di Scienze e Tecnologie Alimentari e Microbiologiche, Sezione di Microbiologia Industriale - Universita degli Studi, Milan, 20133, Italy
SOURCE: Biotechnology Techniques (1998), 12(7), 529-532
CODEN: BTECE6; ISSN: 0951-208X
PUBLISHER: Chapman & Hall
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Lovastatin, mevastatin, pravastatin and monacolin J were produced using Aspergillus terreus strains. Mevastatin (170 mg/L) was obtained at 14 days from the A1 strain, lovastatin (256 mg/L) at 21 days from the A2 strain and pravastatin (270-300 mg/L) at 14 days from both the A1 and A2 strains grown on defatted soybean flour. Similar yields of monacolin J (5-10 mg/L) were detected for both strains. Fermentation carried out by adding glycerol to A1 7-d old cultures gave 244 mg lovastatin/l at 14 days employing whole soybean flour. A new extraction procedure was applied to an A2 19-d old culture on the mycelium and the culture filtrate sep. Recovery yield showed that 83%

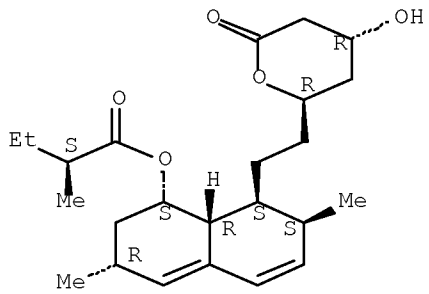
lovastatin was associated with the mycelium and 17% was free in the culture filtrate.

IT 75330-75-5P, Lovastatin
RL: BMF (Bioindustrial manufacture); PUR (Purification or recovery); BIOL (Biological study); PREP (Preparation)
(production and purification of statins from Aspergillus terreus)

RN 75330-75-5 HCAPLUS

CN Butanoic acid, 2-methyl-, (1S,3R,7S,8S,8aR)-1,2,3,7,8,8a-hexahydro-3,7-dimethyl-8-[2-[(2R,4R)-tetrahydro-4-hydroxy-6-oxo-2H-pyran-2-yl]ethyl]-1-naphthalenyl ester, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L91 ANSWER 36 OF 45 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1998:242323 HCAPLUS Full-text

DOCUMENT NUMBER: 129:3880

TITLE: Studies on monacolin K produced by Manascus SPP. II

AUTHOR(S): Mao, Ning; Chen, Xixiang; Yang, Qing; Chen, Songsheng

CORPORATE SOURCE: Bioengineering College, Fujian Teachers University, Fuzhou, 350007, Peop. Rep. China

SOURCE: Fujian Shifan Daxue Xuebao, Ziran Kexueban (1997), 13(4), 80-84
CODEN: FSDKES; ISSN: 1000-5277

PUBLISHER: Fujian Shifan Daxue Xuebao Bianjibu

DOCUMENT TYPE: Journal

LANGUAGE: Chinese

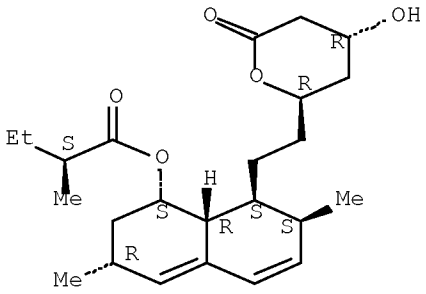
AB Monascus strains were fermented with rice-flour medium and peptone-glucose medium. Three UV absorption peaks at 229, 237, and 247 nm were observed in the fermenting filter liquor. Monacolin K was detected by SiO2 gel TLC in the extractive fermenting liquor. The results showed that optimal media for producing red pigment and Monacolin K are different.

IT 75330-75-5P, Monacolin K
RL: BPN (Biosynthetic preparation); BIOL (Biological study); PREP (Preparation)
(monacolin K produced by Manascus SPP. II)

RN 75330-75-5 HCAPLUS

CN Butanoic acid, 2-methyl-, (1S,3R,7S,8S,8aR)-1,2,3,7,8,8a-hexahydro-3,7-dimethyl-8-[2-[(2R,4R)-tetrahydro-4-hydroxy-6-oxo-2H-pyran-2-yl]ethyl]-1-naphthalenyl ester, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



L91 ANSWER 37 OF 45 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1997:756001 HCAPLUS Full-text
DOCUMENT NUMBER: 128:48073
TITLE: Synthesis of lovastatin with immobilized Candida rugosa lipase in organic solvents: effects of reaction conditions on initial rates
AUTHOR(S): Yang, Fangxiao; Weber, Timothy W.; Gainer, John L.; Carta, Giorgio
CORPORATE SOURCE: Department of Chemical Engineering, University of Virginia, Charlottesville, VA, 22903-2442, USA
SOURCE: Biotechnology and Bioengineering (1997), 56(6), 671-680
CODEN: BIBIAU; ISSN: 0006-3592
PUBLISHER: John Wiley & Sons, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 128:48073

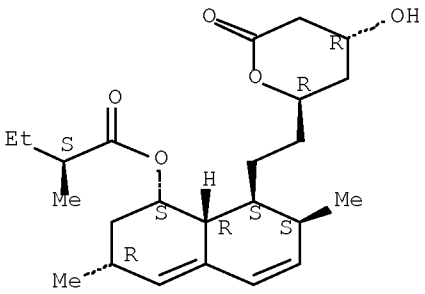
AB Lipase from Candida rugosa immobilized on a nylon support has been used to synthesize lovastatin, a drug which lowers serum cholesterol levels, by the regioselective acylation of a diol lactone precursor with 2-methylbutyric acid in mixts. of organic solvents. Analogs of lovastatin having a different side chain were also obtained through this method by reacting the diol substrate with different carboxylic acids. The selection of reaction conditions that maximize the initial reaction rate is investigated. Since the diol substrate has very low solubility in non-polar solvents, reaction solvents consisting of mixts. of hexane with a different, more polar cosolvent are considered. For each of the cosolvent mixts. studied, the reaction rate is maximum for an intermediate percentage of cosolvent in hexane. With total concns. of the diol lactone in the range 6.25-12.5 mM, maximum initial rates correspond approx. to those cosolvent concns. that permit a complete solubilization of the substrate. At higher cosolvent concns., lower rates are obtained. When considering the same dissolved substrate concentration, the reaction rate was found to increase with increasing values of logPmix and decreasing values of the dielec. constant, when varying the composition of a binary solvent mixture However, when comparing different cosolvents, no general trend with respect to these properties was observed

IT 75330-75-5P, Lovastatin
RL: BPN (Biosynthetic preparation); BIOL (Biological study); PREP (Preparation)
(synthesis and effects of reaction conditions on initial rates of lovastatin with immobilized Candida rugosa lipase in organic solvents)

RN 75330-75-5 HCAPLUS
CN Butanoic acid, 2-methyl-, (1S,3R,7S,8S,8aR)-1,2,3,7,8,8a-hexahydro-3,7-

dimethyl-8-[2-[(2R,4R)-tetrahydro-4-hydroxy-6-oxo-2H-pyran-2-yl]ethyl]-1-naphthalenyl ester, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L91 ANSWER 38 OF 45 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1997:679189 HCAPLUS Full-text
DOCUMENT NUMBER: 127:292132
TITLE: Preparation of microbial polyunsaturated fatty acid containing oil from pasteurized biomass
INVENTOR(S): Bijl, Hendrik Louis; Wolf, Johannes Hendrik; Schaap, Albert; Visser, Johannes Martinus Jacobus
PATENT ASSIGNEE(S): Gist-Brocades, Neth.
SOURCE: PCT Int. Appl., 61 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9737032	A2	19971009	WO 1997-EP1448	19970321
WO 9737032	A3	19971231		
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU				
RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 6255505	B1	20010703	US 1997-821026	19970319
US 2003143659	A1	20030731	US 1997-821025	19970319
CA 2250581	A1	19971009	CA 1997-2250581	19970321
CA 2579516	A1	19971009	CA 1997-2579516	19970321
AU 9721592	A	19971022	AU 1997-21592	19970321
AU 731785	B2	20010405		
EP 894142	A2	19990203	EP 1997-914289	19970321
EP 894142	B1	20060531		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				

CN 1217029	A	19990519	CN 1997-194210	19970321
JP 2000508888	T	20000718	JP 1997-534883	19970321
EP 1369474	A1	20031210	EP 2003-19664	19970321
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
EP 1506996	A2	20050216	EP 2004-27427	19970321
EP 1506996	A3	20060614		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
CN 1715394	A	20060104	CN 2005-10068880	19970321
AT 328104	T	20060615	AT 1997-914289	19970321
ES 2267137	T3	20070301	ES 1997-914289	19970321
IN 1997DE00764	A	20050311	IN 1997-DE764	19970326
ZA 9702702	A	19980327	ZA 1997-2702	19970327
US 2001025114	A1	20010927	US 2001-764087	20010119
US 6441208	B2	20020827		
AU 771809	B2	20040401	AU 2001-33375	20010330
AU 760175	B2	20030508	AU 2001-54159	20010629
US 2004049062	A1	20040311	US 2002-216491	20020809
US 6727373	B2	20040427		
JP 2006000116	A	20060105	JP 2005-180991	20050621
JP 2007270150	A	20071018	JP 2007-108918	20070418

PRIORITY APPLN. INFO.:

EP 1996-200835	A	19960328
EP 1996-200837	A	19960328
US 1996-15086P	P	19960410
US 1996-15110P	P	19960410
US 1997-821026	A1	19970319
AU 1997-21592	A3	19970321
AU 1997-25050	A3	19970321
CA 1997-2250575	A3	19970321
CN 1997-194211	A3	19970321
EP 1997-914289	A3	19970321
EP 1997-916373	A3	19970321
JP 1997-534883	A3	19970321
WO 1997-EP1448	W	19970321
US 2001-764087	A3	20010119

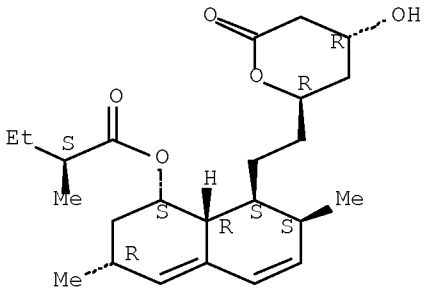
AB The present invention discloses a microbial polyunsatd. fatty acid (PUFA)-containing oil with a high triglyceride content and a high oxidative stability. In addition, a method is described for the recovery of such oil from a microbial biomass derived from a pasteurized fermentation broth, wherein the microbial biomass is subjected to extrusion to form granular particles, dried and the oil then extracted from the dried granules using an appropriate solvent.

IT 75330-75-5P, Lovastatin
RL: BMF (Bioindustrial manufacture); BPN (Biosynthetic preparation); FFD (Food or feed use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of microbial polyunsatd. fatty acid containing oil from pasteurized biomass)

RN 75330-75-5 HCAPLUS

CN Butanoic acid, 2-methyl-, (1S,3R,7S,8S,8aR)-1,2,3,7,8,8a-hexahydro-3,7-dimethyl-8-[2-[(2R,4R)-tetrahydro-4-hydroxy-6-oxo-2H-pyran-2-yl]ethyl]-1-naphthalenyl ester, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



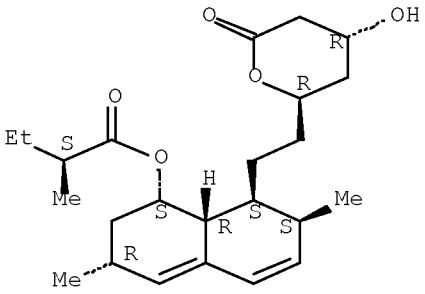
L91 ANSWER 39 OF 45 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1997:606484 HCAPLUS Full-text
DOCUMENT NUMBER: 127:290371
TITLE: Mevinolin production by some fungi
AUTHOR(S): Shindia, A. A.
CORPORATE SOURCE: Botany Department, Faculty of Science, Zagazig University, Egypt
SOURCE: Folia Microbiologica (Prague) (1997), 42(5), 477-480
CODEN: FOMIAZ; ISSN: 0015-5632
PUBLISHER: Institute of Microbiology, Academy of Sciences of the Czech Republic
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The potentiality of 25 fungal species belonging to 14 genera isolated from Egyptian soils to produce mevinolin, a hypocholesterolemic agent, when grown on selected substrates was tested. For the first screening samples of culture filtrates were tested by TLC and the pos. results were further estimated by HPLC anal. It was found that nearly one-third of the tested fungi showed pos. results as to production of mevinolin. Aspergillus terreus was distinguished by its capacity to produce mevinolin when cultivated on a selected medium. The maximum mevinolin yields were achieved after on 8-d incubation at 30°C. An initial pH value of 5-6 was found to be the optimum for growth of A. terreus and mevinolin production

IT 75330-75-5P, Mevinolin
RL: BAC (Biological activity or effector, except adverse); BPN (Biosynthetic preparation); BSU (Biological study, unclassified); BIOL (Biological study); PREP (Preparation)
(mevinolin production by some fungi)

RN 75330-75-5 HCAPLUS
CN Butanoic acid, 2-methyl-, (1S,3R,7S,8S,8aR)-1,2,3,7,8,8a-hexahydro-3,7-dimethyl-8-[2-[(2R,4R)-tetrahydro-4-hydroxy-6-oxo-2H-pyran-2-yl]ethyl]-1-naphthalenyl ester, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L91 ANSWER 40 OF 45 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1997:479354 HCAPLUS Full-text
DOCUMENT NUMBER: 127:94184
TITLE: Method of production of lovastatin
INVENTOR(S): Dimov, Dimcho Ivanov; Grozdanov, Georgy Asenov; Petkov, Nedelcho Genov; Todorova, Dimitra Tsoneva; Dimitrova, Albena Stefanova
PATENT ASSIGNEE(S): Antibiotic Co., Bulg.
SOURCE: PCT Int. Appl., 6 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 9720834	A1	19970612	WO 1996-BG13		19961022
W: AL, AU, BB, BR, CA, CN, CZ, EE, GE, HU, IL, IS, JP, KP, KR, LK, LR, LT, LV, MG, MN, MX, NO, NZ, PL, RO, SG, SI, SK, TR, TT, UA, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM					
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG					
BG 63011	B1	20010131	BG 1996-100316		19960129
CA 2243592	A1	19970612	CA 1996-2243592		19961022
CA 2243592	C	20011225			
AU 9672716	A	19970627	AU 1996-72716		19961022
EP 877742	A1	19981118	EP 1996-934242		19961022
EP 877742	B1	20010816			
R: BE, DE, ES, LU, NL					
ES 2131037	T3	20011216	ES 1996-934242		19961022
PRIORITY APPLN. INFO.:			BG 1995-100197	A	19951206
			BG 1996-100316	A	19960129
			WO 1996-BG13	W	19961022

AB The method finds application in the pharmaceutical industry. Lovastatin is derived by this method from culture broth by filtration at values of pH 9.5-13.0, included in a solid mass it is precipitated from the filtrate obtained, pH 2.5-4.0, in the presence of an inert filler, antioxidant and a non-miscible with water organic solvent. It is extracted and lactonized in the medium of a chlorine-containing organic solvent. The latter is concentrated, and the residue is dissolved in a mixture of solvents having different polarity.

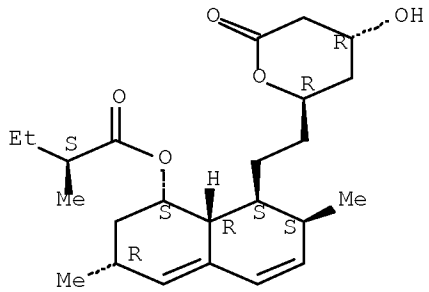
After cooling at -(10-30°), lovastatin is crystallized, dried, and recrystd. several times.

IT 75330-75-5P, Lovastatin
RL: BMF (Bioindustrial manufacture); PUR (Purification or recovery); BIOL (Biological study); PREP (Preparation)
(purification of lovastatin from fermentation broth)

RN 75330-75-5 HCAPLUS

CN Butanoic acid, 2-methyl-, (1S,3R,7S,8S,8aR)-1,2,3,7,8,8a-hexahydro-3,7-dimethyl-8-[2-[(2R,4R)-tetrahydro-4-hydroxy-6-oxo-2H-pyran-2-yl]ethyl]-1-naphthalenyl ester, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



L91 ANSWER 41 OF 45 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1997:119244 HCAPLUS Full-text
DOCUMENT NUMBER: 126:130648
TITLE: Process for recovering water-insoluble compounds from a fermentation broth
INVENTOR(S): Chu, Alexander H. T.; Wloch, Gene P.
PATENT ASSIGNEE(S): Abbott Laboratories, USA
SOURCE: PCT Int. Appl., 21 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9640758	A1	19961219	WO 1996-US9787	19960607
W: CA, JP, MX				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 5616595	A	19970401	US 1995-472615	19950607
CA 2222810	A1	19961219	CA 1996-2222810	19960607
CA 2222810	C	20020212		
EP 832108	A1	19980401	EP 1996-923254	19960607
EP 832108	B1	20000426		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
JP 10511000	T	19981027	JP 1997-502007	19960607
JP 3146010	B2	20010312		
AT 192162	T	20000515	AT 1996-923254	19960607
ES 2146007	T3	20000716	ES 1996-923254	19960607
PT 832108	T	20000831	PT 1996-923254	19960607

GR 3033795	T3	20001031	GR 2000-401494		20000627
PRIORITY APPLN. INFO.:			US 1995-472615	A	19950607
			WO 1996-US9787	W	19960607

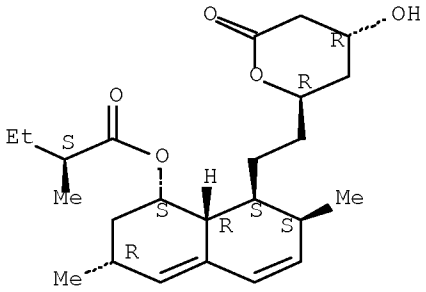
AB A novel process for recovering water-insol. compds. from a fermentation broth including the sequential steps of concentrating, solubilizing and diafiltering the compound of interest, all through a single closed recirculation system to recover the compound for further downstream purification

IT 75330-75-5P, Lovastatin
RL: BMF (Bioindustrial manufacture); PUR (Purification or recovery); BIOL (Biological study); PREP (Preparation)
(recovering water-insol. compds. from a fermentation broth)

RN 75330-75-5 HCAPLUS

CN Butanoic acid, 2-methyl-, (1S,3R,7S,8S,8aR)-1,2,3,7,8,8a-hexahydro-3,7-dimethyl-8-[2-[(2R,4R)-tetrahydro-4-hydroxy-6-oxo-2H-pyran-2-yl]ethyl]-1-naphthalenyl ester, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



L91 ANSWER 42 OF 45 HCAPLUS COPYRIGHT 2007 ACS on STN

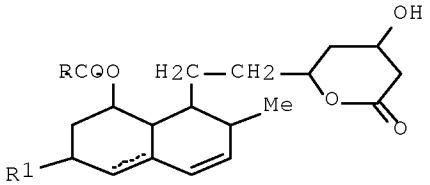
ACCESSION NUMBER:	1995:316101 HCAPLUS Full-text
DOCUMENT NUMBER:	122:263678
TITLE:	Synthesis of hydroxymethylglutaryl-CoA reductase inhibitors
INVENTOR(S):	Carta, Giorgio; Conder, Michael J.; Gainer, John Lloyd; Stieberg, Robert W.; Vinci, Victor A.; Weber, Timothy Wallace
PATENT ASSIGNEE(S):	Merck and Co., Inc., USA; University of Virginia Alumni Patents Foundation
SOURCE:	PCT Int. Appl., 16 pp. CODEN: PIXXD2
DOCUMENT TYPE:	Patent
LANGUAGE:	English
FAMILY ACC. NUM. COUNT:	1
PATENT INFORMATION:	

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9426920	A1	19941124	WO 1994-US5019	19940506
W: AU, BB, BG, BR, BY, CA, CN, CZ, FI, HU, JP, KR, KZ, LK, LV, MG, MN, MW, NO, NZ, PL, RO, RU, SD, SI, SK, TT, UA, US, UZ				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 5420024	A	19950530	US 1993-60847	19930511
CA 2161788	A1	19941124	CA 1994-2161788	19940506

CA 2161788	C	20011016			
AU 9469072	A	19941212	AU 1994-69072		19940506
AU 673268	B2	19961031			
EP 698111	A1	19960228	EP 1994-917312		19940506
EP 698111	B1	20030219			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE					
JP 08510128	T	19961029	JP 1994-525564		19940506
AT 232910	T	20030315	AT 1994-917312		19940506
ES 2190441	T3	20030801	ES 1994-917312		19940506
PRIORITY APPLN. INFO.:			US 1993-60847	A	19930511
			WO 1994-US5019	W	19940506

OTHER SOURCE(S): MARPAT 122:263678

GI



I R = alkyl; R^1 = H, alkyl

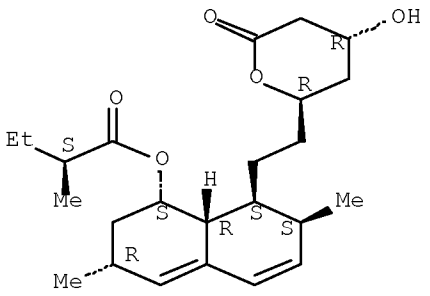
AB HMG-CoA reductase inhibitors of formula (I) are formed by esterification employing an immobilized lipase in a nonaq. organic solvent. Thus, lovastatin diol lactone was incubated with nylon-immobilized lipase type VII from Candida cylindracea and 2-methylbutyric acid in a solvent of 1:1 CHCl3-hexane and shaken at room temperature Lovastatin formation occurred at a rate of 3.2 × 10-5 mol/h-g lipase.

IT 75330-75-5P, Lovastatin
RL: BPN (Biosynthetic preparation); BIOL (Biological study); PREP (Preparation)
(synthesis of hydroxymethylglutaryl-CoA reductase inhibitors with lipase)

RN 75330-75-5 HCAPLUS

CN Butanoic acid, 2-methyl-, (1S,3R,7S,8S,8aR)-1,2,3,7,8,8a-hexahydro-3,7-dimethyl-8-[2-[(2R,4R)-tetrahydro-4-hydroxy-6-oxo-2H-pyran-2-yl]ethyl]-1-naphthalenyl ester, (2S)- (CA INDEX NAME)

Absolute stereochemistry.

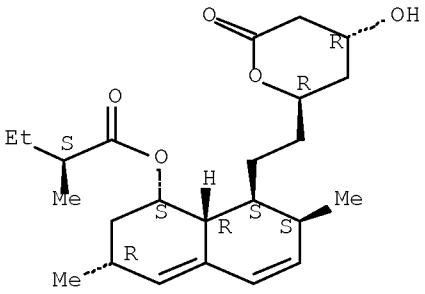


L91 ANSWER 43 OF 45 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1993:154452 HCAPLUS Full-text
DOCUMENT NUMBER: 118:154452
TITLE: Applications of supercritical fluids in the controlled release of drugs
AUTHOR(S): Tom, Jean W.; Lim, Gio Bin; Debenedetti, Pablo G.; Prud'homme, Robert K.
CORPORATE SOURCE: Dep. Chem. Eng., Princeton Univ., Princeton, NJ, 08544, USA
SOURCE: ACS Symposium Series (1993), 514(Supercritical Fluid Engineering Science), 238-57
CODEN: ACSMC8; ISSN: 0097-6156
DOCUMENT TYPE: Journal
LANGUAGE: English

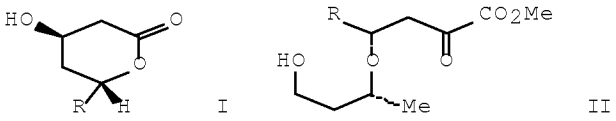
AB Supercrit. fluids have been used to form two different types of microparticles intended for controlled drug release applications: drug-loaded polymer microspheres, and small protein particles. A poly(hydroxyacid), poly(DL-lactic acid) (DL-PLA) and a pharmaceutical (lovastatin) have been dissolved in supercrit. CO2 and copptd. by rapid expansion of the resulting supercrit. solution (RESS) to form polymer-drug microspheres and microparticles ranging in size from 10 to 100 μm. Variations in the concentration of lovastatin in the precipitate correlated with changes in the precipitate's morphol., ranging from continuous drug-polymer networks, to microparticles, to microspheres. The formation of polymer-drug microparticles by RESS is the first step towards a feasible single-step, low-temperature process that yields solvent and surfactant-free microparticles suitable for controlled drug release. Two model proteins, catalase and insulin, have been dissolved in ethanol/water solution and fed continuously and simultaneously with supercrit. CO2 into a crystallizer to precipitate the proteins. The use of supercrit. CO2 as a gas anti-solvent (GAS) produced catalase and insulin particles ranging from 1 to 5 μm. Particle morphol. ranged from microspheres, to rectangular-shaped particles, to needles. Micron-sized protein particles are needed in several controlled-release formulations to accommodate the high potency and low dosage of such pharmaceuticals and to achieve a uniform dispersion of the drug in the injectable polymeric microspherical carrier. GAS crystallization is a potentially important process for comminution of proteins since conventional particle reduction methods (spray drying, lyophilization, milling, grinding) cannot produce the micron-sized protein particles needed for controlled release of highly active enzymes.

IT 75330-75-5P, Lovastatin
RL: SPN (Synthetic preparation); PREP (Preparation)
(microparticles for controlled release of, supercrit. fluids in preparation of)
RN 75330-75-5 HCAPLUS
CN Butanoic acid, 2-methyl-, (1S,3R,7S,8S,8aR)-1,2,3,7,8,8a-hexahydro-3,7-dimethyl-8-[2-[(2R,4R)-tetrahydro-4-hydroxy-6-oxo-2H-pyran-2-yl]ethyl]-1-naphthalenyl ester, (2S)- (CA INDEX NAME)

Absolute stereochemistry.

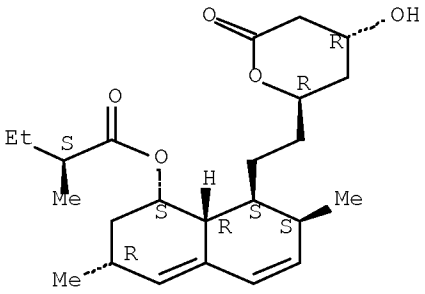


L91 ANSWER 44 OF 45 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1989:231315 HCAPLUS Full-text
DOCUMENT NUMBER: 110:231315
TITLE: Asymmetric synthesis via acetal templates. 15. The preparation of enantiomerically pure mevinolin analogs
AUTHOR(S): Johnson, William S.; Kelson, Andrew B.; Elliott, John D.
CORPORATE SOURCE: Dep. Chem., Stanford Univ., Stanford, CA, 94305, USA
SOURCE: Tetrahedron Letters (1988), 29(31), 3757-60
CODEN: TELEAY; ISSN: 0040-4039
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 110:231315
GI



AB An efficient asym. synthesis of the hydroxy acetone moiety I [R = 2,4,6-Cl2(4-FC6H4)C6H2CH:CH, 2-cyclohexylethyl] of mevinolin. The key step is the TiCl4-catalyzed coupling reaction of acetals derived from (R)-1,3-butanediol with Me3SiOC(:CH2)CH:C(OMe)OSiMe3 to give the δ-alkoxy-β-keto esters II.
IT 75330-75-5DP, Mevinolin, analogs
RL: PREP (Preparation)
(asym. preparation of)
RN 75330-75-5 HCAPLUS
CN Butanoic acid, 2-methyl-, (1S,3R,7S,8S,8aR)-1,2,3,7,8,8a-hexahydro-3,7-dimethyl-8-[2-[(2R,4R)-tetrahydro-4-hydroxy-6-oxo-2H-pyran-2-yl]ethyl]-1-naphthalenyl ester, (2S)- (CA INDEX NAME)

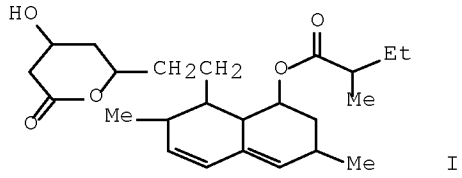
Absolute stereochemistry.



L91 ANSWER 45 OF 45 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1981:119471 HCAPLUS Full-text
DOCUMENT NUMBER: 94:119471
ORIGINAL REFERENCE NO.: 94:19535a,19538a
TITLE: Monacolin K
INVENTOR(S): Tsujita, Yoshio; Tanzawa, Kazuhiko; Furuya, Kohei; Masao, Kuroda; Iwado, Seigo
PATENT ASSIGNEE(S): Sankyo Co., Ltd., Japan
SOURCE: Ger. Offen., 23 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 3006215	A1	19801127	DE 1980-3006215	19800220
DE 3006215	C2	19890105		
JP 55150898	A	19801125	JP 1979-57927	19790511
DK 8000731	A	19801112	DK 1980-731	19800220
DK 148807	B	19851007		
DK 148807	C	19860428		
SE 8001338	A	19801112	SE 1980-1338	19800220
SE 467975	B	19921012		
SE 467975	C	19930218		
CH 645891	A5	19841031	CH 1980-1367	19800220
DE 3051097	C2	19900208	DE 1980-3051097	19800220
GB 2049664	A	19801231	GB 1980-7240	19800304
GB 2049664	B	19830112		
BE 882325	A1	19800919	BE 1980-199871	19800319
AT 8001482	A	19830415	AT 1980-1482	19800319
AT 372975	B	19831212		
FR 2456141	A1	19801205	FR 1980-6203	19800320
FR 2456141	B1	19831118		
CA 1129795	A1	19820817	CA 1980-348220	19800320
AU 8056678	A	19801113	AU 1980-56678	19800321
AU 534647	B2	19840209		
NL 8001697	A	19801113	NL 1980-1697	19800321
HU 24471	A2	19830228	HU 1980-679	19800321
HU 182075	B	19831228		
US 4323648	A	19820406	US 1980-137821	19800404
SE 8701483	A	19881010	SE 1987-1483	19870409
SE 468482	B	19930125		

SE 468482 C 19930519
PRIORITY APPLN. INFO.: JP 1979-57927 A 19790511
GI



I

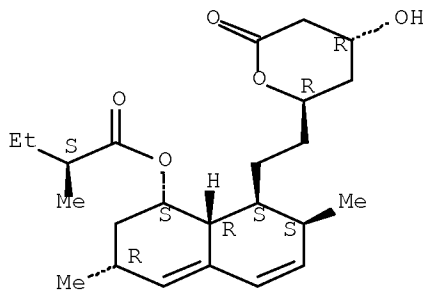
AB Monacolin K (I) [71949-96-7] is produced by fermentation with Monascus. Thus, 300 L medium containing soluble starch 1.5, glycerol 1.5, fish meal 2, and CaCO3 0.2% was inoculated with M. ruber FERM 4957 and incubated at 27° for 5 days with aeration and stirring. The broth was filtered and the filtrate was extracted with EtOAc and the extract concentrated to an oil. The mycelium was extracted with 80% aqueous MeOH. The MeOH was evaporated off, the extract extracted with EtOAc, and the EtOAc extract concentrated to an oil. The oils from the filtrate and mycelium (223 g) were combined and chromatographed 3 times on silica gel. The last step yielded an active fraction that was concentrated to yield 54 mg I crystal.

IT 75330-75-5P
RL: BMF (Bioindustrial manufacture); BIOL (Biological study); PREP (Preparation)
(manufacture of, with Monascus)

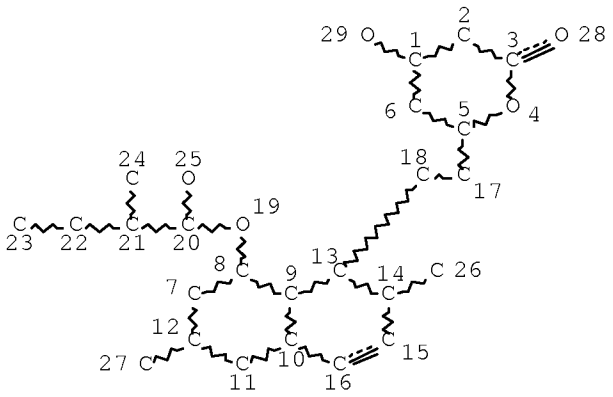
RN 75330-75-5 HCAPLUS

CN Butanoic acid, 2-methyl-, (1S,3R,7S,8S,8aR)-1,2,3,7,8,8a-hexahydro-3,7-dimethyl-8-[2-[(2R,4R)-tetrahydro-4-hydroxy-6-oxo-2H-pyran-2-yl]ethyl]-1-naphthalenyl ester, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



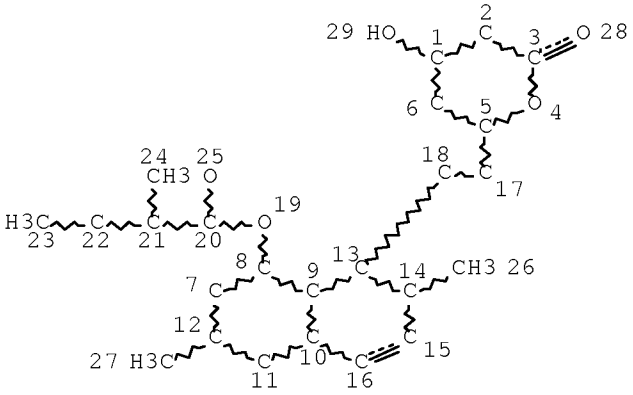
=> => D STAT QUE L99
L56 STR



NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 29

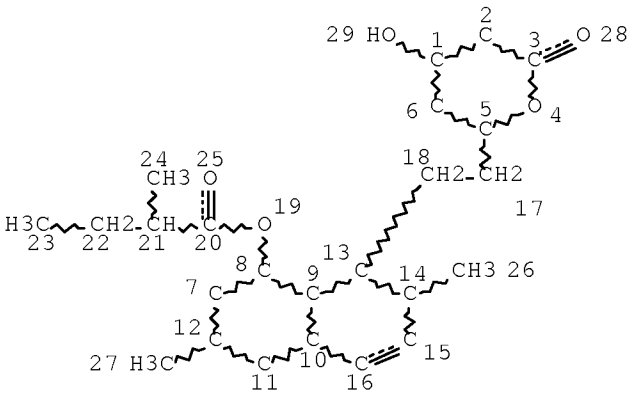
STEREO ATTRIBUTES: NONE
L58 336 SEA FILE=REGISTRY SSS FUL L56
L59 STR



NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 29

STEREO ATTRIBUTES: NONE
L60 145 SEA FILE=REGISTRY SUB=L58 SSS FUL L59
L61 STR



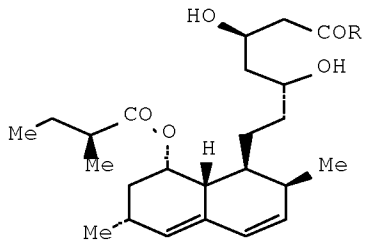
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 29

STEREO ATTRIBUTES: NONE

L63		SCR 2127
L64	33	SEA FILE=REGISTRY SUB=L58 SSS FUL L61 NOT L63
L65	3561	SEA FILE=HCAPLUS ABB=ON PLU=ON L64
L66	1	SEA FILE=REGISTRY ABB=ON PLU=ON "MEVINOLINIC ACID"/CN
L67		SEL PLU=ON L66 1- CHEM : 10 TERMS
L68	162	SEA FILE=HCAPLUS ABB=ON PLU=ON L67
L69	164	SEA FILE=HCAPLUS ABB=ON PLU=ON L68 OR MEVINOLINIC(W)ACID OR MEVINOLINATE
L70	119	SEA FILE=HCAPLUS ABB=ON PLU=ON L65 AND L69
L74	328	SEA FILE=HCAPLUS ABB=ON PLU=ON L65(L)(BMF OR PREP OR BPN)/RL
L75	30	SEA FILE=HCAPLUS ABB=ON PLU=ON L70 AND L74
L79	18	SEA FILE=REGISTRY ABB=ON PLU=ON MINERAL(L)ACID OR SULFONIC ACID/CN OR NITRIC ACID/CN OR ORTHOPHOSPHORIC ACID/CN OR HYDROCHLORIC ACID/CN
L80	1	SEA FILE=REGISTRY ABB=ON PLU=ON ORTHOPHOSPHORIC ACID/CN
L81	72933	SEA FILE=HCAPLUS ABB=ON PLU=ON L80
L82	399316	SEA FILE=HCAPLUS ABB=ON PLU=ON L79 OR (MINERAL OR SULFURIC OR NITRIC OR L81 OR HYDROCHLORIC)(W) ACID
L83	15	SEA FILE=HCAPLUS ABB=ON PLU=ON L74 AND L82
L84	1388	SEA FILE=REGISTRY ABB=ON PLU=ON SOLVENT OR SOLVENTS OR HYDROCARBONS/CN
L86	1959522	SEA FILE=HCAPLUS ABB=ON PLU=ON L83 OR L84 OR SOLVENT OR HYDROCARBON OR ?DICHLOROMETHANE OR CHLOROFORM OR ISOPROPANOL OR ALUMINA OR ACETONE
L87	233	SEA FILE=HCAPLUS ABB=ON PLU=ON L65 AND L86
L88	48	SEA FILE=HCAPLUS ABB=ON PLU=ON L87 AND L74
L89	80	SEA FILE=HCAPLUS ABB=ON PLU=ON L65 AND (FILT? OR ?CRYSTALI? OR EVAPORA?)
L90	29	SEA FILE=HCAPLUS ABB=ON PLU=ON L89 AND L74
L91	45	SEA FILE=HCAPLUS ABB=ON PLU=ON (L83 OR L88 OR L90) NOT L75
L92	112	SEA FILE=REGISTRY ABB=ON PLU=ON L60 NOT L64

```
L93         133 SEA FILE=REGISTRY ABB=ON  PLU=ON  L92 OR LOVASTATIN
L94        6902 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L93 OR LOVASTATIN
L95         462 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L94(L)(BMF OR PREP OR BPN)/RL

L97          60 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L95 AND L69
L98          23 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L97 AND L86
L99          10 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L98 NOT (L75 OR L91)


=> D IBIB ABS HITSTR L99 1-10

L99  ANSWER 1 OF 10  HCAPLUS  COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER:         2005:118935  HCAPLUS  Full-text
DOCUMENT NUMBER:          142:154347
TITLE:                    An improved process for the preparation of
                          mevinolinic acid or its salt
INVENTOR(S):              Vaid, Sudhir; Maurya, Rajkumar; Sharma, Sunita;
                          Upadhyay, Girish Chandra
PATENT ASSIGNEE(S):       Ranbaxy Laboratories Ltd., India
SOURCE:                   Indian, 11 pp.
                          CODEN: INXXAP
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.           KIND   DATE        APPLICATION NO.         DATE
     ---------------      ----   --------    --------------------    --------
     IN 185764             A1    20010428    IN 1997-DE1500          19970605
PRIORITY APPLN. INFO.:                       IN 1997-DE1500          19970605
OTHER SOURCE(S):          CASREACT 142:154347
GI
```



I

AB An improved process was disclosed for the preparation of mevinolinic acid I (R = OH) and its ammonium salt I (R = O-N+H4) and was comprised of fermentation by a microfungus of genus Aspergillus in conventional culture media, addition of an assimilable carbon source, either continuously or in calculated batches during fermentation, maintaining the pH of the fermentation broth between 5.5 to 7.5. and maintaining the residual sugar level in the fermentation broth between 0.1 to 2.8%, acidification of the fermentation broth mixed with extraction solvent, refluxing at 60℃ to obtain mevinolinic acid, and finally if desired, conversion to its salt.

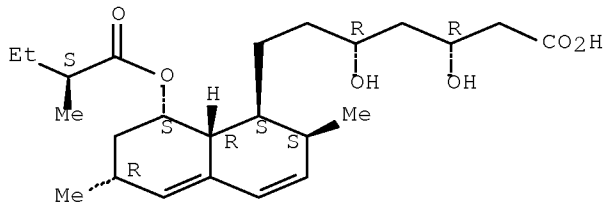
IT 75225-51-3P, Mevinolinic acid

RL: BMF (Bioindustrial manufacture); BPN (Biosynthetic preparation); BIOL (Biological study); PREP (Preparation)
(fermentation process for the preparation of mevinolinic acid and its ammonium salt)

RN 75225-51-3 HCAPLUS

CN 1-Naphthaleneheptanoic acid, 1,2,6,7,8,8a-hexahydro-β,δ-dihydroxy-2,6-dimethyl-8-[(2S)-2-methyl-1-oxobutoxy]-, (βR,δR,1S,2S,6R,8S,8aR)- (CA INDEX NAME)

Absolute stereochemistry.

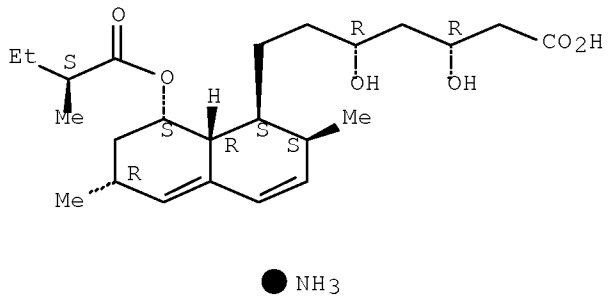


IT 77550-67-5P, Mevinolinic acid ammonium salt
RL: BMF (Bioindustrial manufacture); BPN (Biosynthetic preparation); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(fermentation process for the preparation of mevinolinic acid and its ammonium salt)

RN 77550-67-5 HCAPLUS

CN 1-Naphthaleneheptanoic acid, 1,2,6,7,8,8a-hexahydro-β,δ-dihydroxy-2,6-dimethyl-8-[(2S)-2-methyl-1-oxobutoxy]-, ammonium salt (1:1), (βR,δR,1S,2S,6R,8S,8aR)- (CA INDEX NAME)

Absolute stereochemistry.

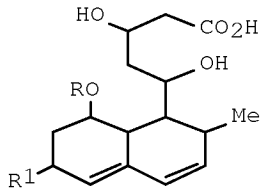


L99 ANSWER 2 OF 10 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:8511 HCAPLUS Full-text
DOCUMENT NUMBER: 142:71651
TITLE: A novel process for the purification of antihypercholesterolemic agents from fermented wet biomass
INVENTOR(S): Venkatesh, Needamangalam Sriniv; Ganesh, Sambasivam
PATENT ASSIGNEE(S): Helix Biotech Pvt Ltd., India

SOURCE: Indian, 17 pp.
CODEN: INXXAP
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
IN 184324	A1	20000805	IN 1996-MA2202	19961206

PRIORITY APPLN. INFO.: IN 1996-MA2202 19961206
GI



I

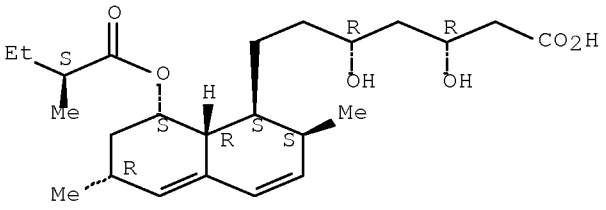
AB This invention pertains to a novel process for the purification of antihypercholesterolemic agents such as mevinolinic acid (I; R = COCHMeEt, R1 = H), triol acid (I; R = H, R1 = Me) and mevinic acid (I; R = COCHMeEt, R1 = Me) from fermented wet biomass. The process comprises the steps of: (i) obtaining a biomass from a sterilized mixture of solid materials (e.g., wheat, bran, maize) in water, which was inoculated with a well grown culture of Aspergillus flavipes and fermented under humid conditions at 30° for 5 d.; (ii) extracting the biomass from step (i) with H2O or aqueous solution (of acetone, C1-4-alc., Na2CO3, NaOH, Na3BO3) as described herein and then concentrating the solution; (iii) acidifying the aqueous concentrate of step (ii) with an inorg. acid (HCl, H2SO4) in the presence of H2O immiscible solvents (e.g., EtOAc, CHCl3, CH2Cl2, ClCH2CH2Cl, Et2O); (iv) washing the immiscible solvent from (iii) with an aqueous base (e.g., NaHCO3, KHCO3, Na2CO3) followed by a brine wash; (v) concentrating the extract so obtained under educed pressure to afford the product, I, with antihypercholesterolemic properties.

IT 75225-51-3P, Mevinolinic acid
RL: NPO (Natural product occurrence); PUR (Purification or recovery); BIOL (Biological study); OCCU (Occurrence); PREP (Preparation)
(novel process for the purification of antihypercholesterolemic agents from fermented wet biomass)

RN 75225-51-3 HCAPLUS

CN 1-Naphthaleneheptanoic acid, 1,2,6,7,8,8a-hexahydro-β,δ-dihydroxy-2,6-dimethyl-8-[(2S)-2-methyl-1-oxobutoxy]-, (βR,δR,1S,2S,6R,8S,8aR)- (CA INDEX NAME)

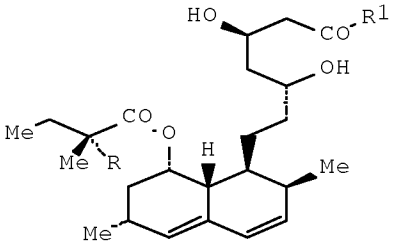
Absolute stereochemistry.



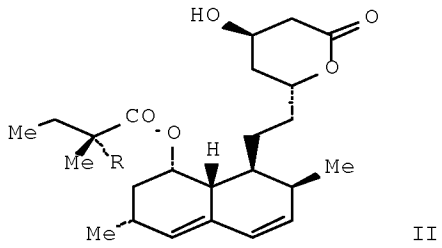
L99 ANSWER 3 OF 10 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:515874 HCAPLUS Full-text
DOCUMENT NUMBER: 141:23344
TITLE: A novel process for the preparation of 2,2-dimethylbutanoic acid (1S,3R,7S,8S,8aR)-8-[(3R,5R)-7-(cyclopropylamino)-3,5-dihydroxy-7-oxoheptyl]-1,2,3,7,8,8a-hexahydro-3,7-dimethyl-1-naphthalenyl ester
INVENTOR(S): Khanna, Jag Mohan; Kumar, Yatendra; Thaper, Rajesh Kumar; Misra, Satya Nand; Kumar, Saridi Madhave Dileep
PATENT ASSIGNEE(S): Ranbaxy Laboratories Ltd., India
SOURCE: Indian, 9 pp.
CODEN: INXXAP
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
IN 184809	A1	20000930	IN 1996-DE1683	19960530
AU 9721409	A	19980129	AU 1997-21409	19970514
AU 692409	B2	19980604		
CN 1173488	A	19980218	CN 1997-111497	19970530
CN 1101805	B	20030219		
HR 970436	B1	20030630	HR 1997-436	19970807
TW 449577	B	20010811	TW 1997-86111653	19970814

PRIORITY APPLN. INFO.: IN 1996-DE1683 A 19960530
US 1997-816574 A 19970313
OTHER SOURCE(S): MARPAT 141:23344
GI



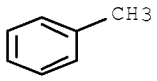
I



II

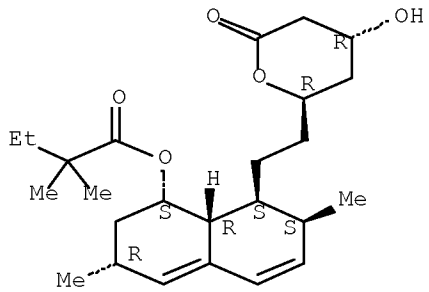
AB A novel process was described for the preparation of the title amide I (R = Me, R1 = cyclopropylamino), a simvastatin II (R = Me) precursor, which comprised reactions of mevinolinic acid salts, such as I (R = H; R1 = O-.N+H4, O-.Na+, or O-.K+) or lovastatin II (R = H) with cyclopropyl amine, and subsequent methylation of the intermediate amide I (R = H, R1 = cyclopropylamino) with MeI in the presence of lithium pyrrolidide.

IT 108-88-3, Toluene, uses
RL: NUU (Other use, unclassified); USES (Uses)
(process for the preparation of the Simvastatin precursor, 2,2-dimethylbutanoic acid (1S,3R,7S,8S,8aR)-8-[(3R,5R)-7-(cyclopropylamino)-3,5-dihydroxy-7-oxoheptyl]-1,2,3,7,8,8a-hexahydro-3,7-dimethyl-1-naphthalenyl ester, via an amidation reaction)
RN 108-88-3 HCAPLUS
CN Benzene, methyl- (CA INDEX NAME)



IT 79902-63-9P, Simvastatin
RL: PNU (Preparation, unclassified); PREP (Preparation)
(process for the preparation of the Simvastatin precursor, 2,2-dimethylbutanoic acid (1S,3R,7S,8S,8aR)-8-[(3R,5R)-7-(cyclopropylamino)-3,5-dihydroxy-7-oxoheptyl]-1,2,3,7,8,8a-hexahydro-3,7-dimethyl-1-naphthalenyl ester, via an amidation reaction)
RN 79902-63-9 HCAPLUS
CN Butanoic acid, 2,2-dimethyl-, (1S,3R,7S,8S,8aR)-1,2,3,7,8,8a-hexahydro-3,7-dimethyl-8-[2-[(2R,4R)-tetrahydro-4-hydroxy-6-oxo-2H-pyran-2-yl]ethyl]-1-naphthalenyl ester (CA INDEX NAME)

Absolute stereochemistry.

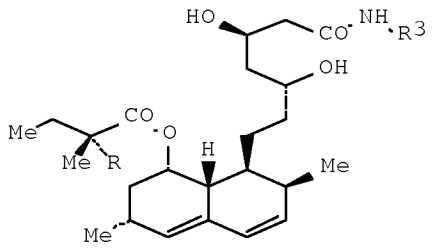


L99 ANSWER 4 OF 10 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:479722 HCAPLUS Full-text
DOCUMENT NUMBER: 141:6967
TITLE: Process for the preparation of simvastatin from lovastatin or mevinolinic acid
INVENTOR(S): Kumar, Yatindra; Thaper, Rajesh Kumar; Misra, Satya Nand; Kumar, S. M. Dileep; Khanna, Jag Mohan

PATENT ASSIGNEE(S): Ranbaxy Laboratories Limited, India
SOURCE: Indian, 12 pp.
CODEN: INXXAP
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
IN 184969	A1	20001014	IN 1997-DE175		19970124
HR 970435	B1	20011231	HR 1997-435		19970807
CZ 290672	B6	20020911	CZ 1997-2649		19970820
SK 283319	B6	20030603	SK 1997-1167		19970825
PRIORITY APPLN. INFO.:			IN 1997-CA175	A	19970124
			IN 1997-DE175	A	19970124
			US 1997-816573	A	19970313

OTHER SOURCE(S): CASREACT 141:6967; MARPAT 141:6967
GI



I

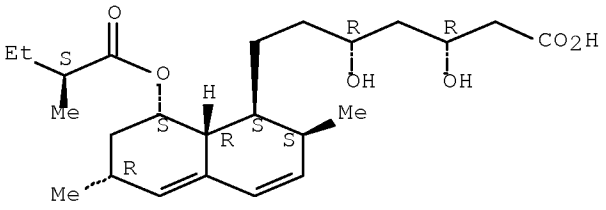
AB A novel process was disclosed for the preparation of simvastatin which comprised reacting lovastatin or mevinolinic acid with alkylamine of the formula R3NH2 (R3 = Bu, cyclopropyl, alkyl) to yield alkyl amide compds. I (R = H, Me; R3 = Bu, cyclopropyl, alkyl) which were then reacted with a methylating agent like MeI in the presence of a base like lithium pyrrolide to give I (R = Me; R3 = Bu, cyclopropyl, alkyl) which are further reacted with a strong base like sodium hydroxide to cleave the amide linkage and then treated with ammonium hydroxide to precipitate simvastatin ammonium salt which on further heating with an organic solvent give simvastatin.

IT 75225-51-3, Mevinolinic acid
RL: RCT (Reactant); RACT (Reactant or reagent)
(claimed starting material; process for the preparation of simvastatin from lovastatin or mevinolinic acid)

RN 75225-51-3 HCAPLUS

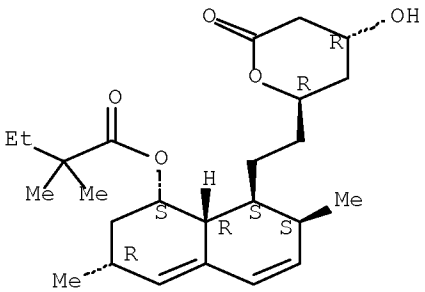
CN 1-Naphthaleneheptanoic acid, 1,2,6,7,8,8a-hexahydro-β,δ-dihydroxy-2,6-dimethyl-8-[(2S)-2-methyl-1-oxobutoxy]-, (βR,δR,1S,2S,6R,8S,8aR)- (CA INDEX NAME)

Absolute stereochemistry.

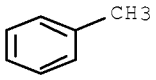


IT 79902-63-9P, Simvastatin
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(process for the preparation of simvastatin from lovastatin or mevinolinic acid)
RN 79902-63-9 HCAPLUS
CN Butanoic acid, 2,2-dimethyl-, (1S,3R,7S,8S,8aR)-1,2,3,7,8,8a-hexahydro-3,7-dimethyl-8-[2-[(2R,4R)-tetrahydro-4-hydroxy-6-oxo-2H-pyran-2-yl]ethyl]-1-naphthalenyl ester (CA INDEX NAME)

Absolute stereochemistry.



IT 108-88-3, Toluene, uses
RL: NUU (Other use, unclassified); USES (Uses)
(process for the preparation of simvastatin from lovastatin or mevinolinic acid)
RN 108-88-3 HCAPLUS
CN Benzene, methyl- (CA INDEX NAME)



L99 ANSWER 5 OF 10 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:813799 HCAPLUS Full-text
DOCUMENT NUMBER: 141:3475
TITLE: Preparation of Mevinolinic Acid from Monascus purpureus Using High-Speed Countercurrent Chromatography (HSCCC)
AUTHOR(S): Du, Qizhen; Xia, Ming; Ito, Yoichiro

CORPORATE SOURCE: Institute of Food and Biological Engineering, Hangzhou University of Commerce, Hangzhou, Peop. Rep. China
SOURCE: Journal of Liquid Chromatography & Related Technologies (2003), 26(18), 3085-3092
CODEN: JLCTFC; ISSN: 1082-6076
PUBLISHER: Marcel Dekker, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

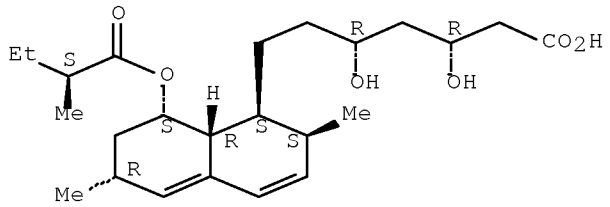
AB High-speed countercurrent chromatog. (HSCCC) was applied for the separation of a crude Monascus purpureus extract The separation was carried out using a two-phase solvent system composed of n-hexane/ethyl acetate/methanol/water (1/1/1/1, volume/volume) at a flow rate of 1.0 mL/min. From 250 mg of the alkaline treated extract the method yielded 40 mg of mevinolinic acid with a purity of 99% in each separation The product was confirmed as mevinolinic acid by electrospray ionization multiple mass spectrometry (ESI-MS) and NMR anal.

IT 75225-51-3P, Mevinolinic acid
RL: PUR (Purification or recovery); PREP (Preparation)
(preparative separation of mevinolinic acid from Monascus purpureus extract using high-speed countercurrent chromatog.)

RN 75225-51-3 HCAPLUS

CN 1-Naphthaleneheptanoic acid, 1,2,6,7,8,8a-hexahydro-β,δ-dihydroxy-2,6-dimethyl-8-[(2S)-2-methyl-1-oxobutoxy]-, (βR,δR,1S,2S,6R,8S,8aR)- (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L99 ANSWER 6 OF 10 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1998:527327 HCAPLUS Full-text
DOCUMENT NUMBER: 129:161450
TITLE: Process for the production of semisynthetic statins via novel intermediates
INVENTOR(S): Vries, Ton Rene; Wijnberg, Hans; Faber, Wijnand Sjourd; Kalkman-Agayn, Venetka Ivanova; Sibeyn, Mieke
PATENT ASSIGNEE(S): Gist-Brocades B.V., Neth.
SOURCE: PCT Int. Appl., 44 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

WO 9832751		A1	19980730	WO 1998-EP519	19980127
W:	AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW				
RW:	GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2278603		A1	19980730	CA 1998-2278603	19980127
AU 9866183		A	19980818	AU 1998-66183	19980127
AU 747219		B2	20020509		
EP 971913		A1	20000119	EP 1998-908031	19980127
EP 971913		B1	20030416		
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
NZ 336993		A	20000526	NZ 1998-336993	19980127
JP 2001508782		T	20010703	JP 1998-531620	19980127
AT 237605		T	20030515	AT 1998-908031	19980127
IL 131044		A	20030731	IL 1998-131044	19980127
PT 971913		T	20030829	PT 1998-908031	19980127
EP 1340752		A1	20030903	EP 2003-8084	19980127
EP 1340752		B1	20060419		
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
ES 2197465		T3	20040101	ES 1998-908031	19980127
AT 323689		T	20060515	AT 2003-8084	19980127
ES 2266671		T3	20070301	ES 2003-8084	19980127
IN 188004		A1	20020803	IN 1998-DE242	19980128
NO 9903644		A	19990928	NO 1999-3644	19990727
NO 318146		B1	20050207		
US 6294680		B1	20010925	US 2000-341809	20000105
IN 194720		A1	20041127	IN 2002-DE90	20020201
IN 2002DE00089		A	20051223	IN 2002-DE89	20020201
IN 2003DE00979		A	20050225	IN 2003-DE979	20030808
IN 2004DE02216		A	20060908	IN 2004-DE2216	20041108
PRIORITY APPLN. INFO.:				EP 1997-200223	A 19970128
				EP 1997-306809	A 19970903
				EP 1998-908031	A3 19980127
				WO 1998-EP519	W 19980127
				IN 1998-DE242	A3 19980128
				IN 2002-DE89	A3 20020201
				IN 2002-DE90	A3 20020201

OTHER SOURCE(S): CASREACT 129:161450; MARPAT 129:161450
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB A process for the production of semisynthetic statins I [R1, R2 = H, OH, alkyl, aryl, arylalkyl; R3 = H, COR9; R4, R5 = H, alkyl, cycloalkyl, alkenyl, alkynyl, Ph, phenylalkyl; NR4R5 = cyclic amine; R6, R7 = H; R6R7 = BR8, CR10R11, P(O)OR12, SO2; R8 = (un)substituted Ph; R9 = (un)substituted alkyl, cycloalkyl, alkenyl, alkynyl, Ph, phenylalkyl; R10, R11 = H (but not both), (un)substituted alkyl, cycloalkyl, alkenyl, alkynyl, Ph, phenylalkyl; R12 = H, alkyl, cycloalkyl, Ph, phenylalkyl, amine (with R3 = H); dashed lines = single

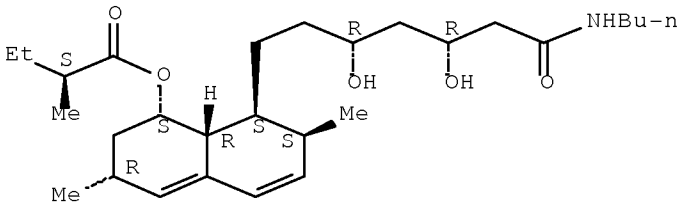
or double bonds] is described. Thus, simvastatin (II) was prepared from lovastatin (III) via ring opening with BuNH2 in PhMe followed by ketalization with acetone containing catalytic p-TsOH; th resulting acetonide is reduced with LiAlH4 in THF; the resulting alc. is acylated with EtCMe2COCl in pyridine containing DMAP followed by heating in aqueous THF containing catalytic p-TsOH and ammoniation with NH4OH in MeOH/EtOH; the resulting ammonium salt is heated to give II.

IT 134970-29-9P, Lovastatin butylamide
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(semisynthesis of statins via novel intermediates)

RN 134970-29-9 HCAPLUS

CN Butanoic acid, 2-methyl-, (1S,3R,7S,8S,8aR)-8-[(3R,5R)-7-(butylamino)-3,5-dihydroxy-7-oxoheptyl]-1,2,3,7,8,8a-hexahydro-3,7-dimethyl-1-naphthalenyl ester, (2S)- (CA INDEX NAME)

Absolute stereochemistry.

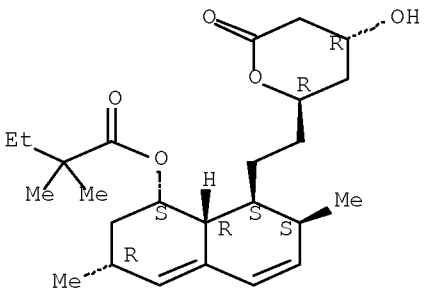


IT 79902-63-9P, Simvastatin 118159-61-8P, Lovastatin acid amide 210980-52-2P, Lovastatin piperidinamide
RL: SPN (Synthetic preparation); PREP (Preparation)
(semisynthesis of statins via novel intermediates)

RN 79902-63-9 HCAPLUS

CN Butanoic acid, 2,2-dimethyl-, (1S,3R,7S,8S,8aR)-1,2,3,7,8,8a-hexahydro-3,7-dimethyl-8-[2-[(2R,4R)-tetrahydro-4-hydroxy-6-oxo-2H-pyran-2-yl]ethyl]-1-naphthalenyl ester (CA INDEX NAME)

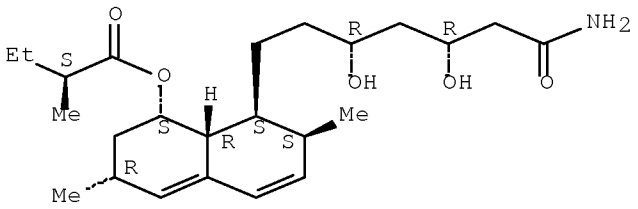
Absolute stereochemistry.



RN 118159-61-8 HCAPLUS

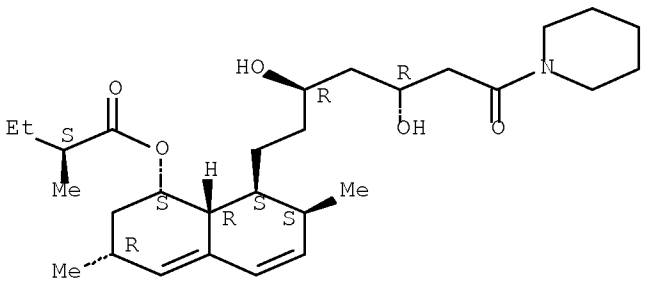
CN Butanoic acid, 2-methyl-, (1S,3R,7S,8S,8aR)-8-[(3R,5R)-7-amino-3,5-dihydroxy-7-oxoheptyl]-1,2,3,7,8,8a-hexahydro-3,7-dimethyl-1-naphthalenyl ester, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



RN 210980-52-2 HCAPLUS
CN Butanoic acid, 2-methyl-, (1S,3R,7S,8S,8aR)-8-[(3R,5R)-3,5-dihydroxy-7-oxo-7-(1-piperidinyl)heptyl]-1,2,3,7,8,8a-hexahydro-3,7-dimethyl-1-naphthalenyl ester, (2S)- (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

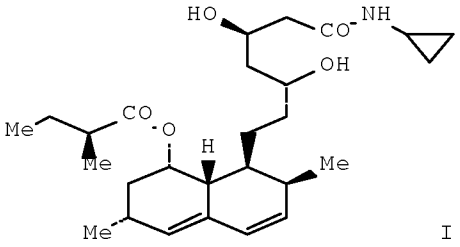
L99 ANSWER 7 OF 10 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1998:397824 HCAPLUS Full-text
DOCUMENT NUMBER: 129:67647
TITLE: Process for manufacturing simvastatin from lovastatin or mevinolinic acid
INVENTOR(S): Kumar, Yatendra; Thaper, Rajesh Kumar; Misra, Satyananda; Kumar, S. M. Dileep; Khanna, Jag Mohan
PATENT ASSIGNEE(S): Ranbaxy Laboratories, Ltd., India
SOURCE: U.S., 7 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5763646	A	19980609	US 1997-816573	19970313
ZA 9704023	A	19971210	ZA 1997-4023	19970509
AU 693401	B1	19980625	AU 1997-21408	19970514
CN 1188763	A	19980729	CN 1997-111494	19970530

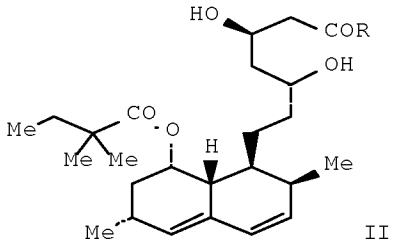
CN 1102588	B	20030305			
EP 864569	A1	19980916	EP 1997-111277		19970704
EP 864569	B1	20010816			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO					
AT 204271	T	20010915	AT 1997-111277		19970704
ES 2162165	T3	20011216	ES 1997-111277		19970704
HR 970435	B1	20011231	HR 1997-435		19970807
TW 427968	B	20010401	TW 1997-86111652		19970814
CZ 290672	B6	20020911	CZ 1997-2649		19970820
SK 283319	B6	20030603	SK 1997-1167		19970825
PRIORITY APPLN. INFO.:			IN 1997-CA175	A	19970124
			IN 1997-DE175	A	19970124
			US 1997-816573	A	19970313

OTHER SOURCE(S): CASREACT 129:67647; MARPAT 129:67647

GI



I



II

AB A process for preparing simvastatin from lovastatin or mevinolinic acid salt without protecting and deprotecting the two hydroxy groups of the open pyranone ring was described. Thus, mevinolinic acid ammonium salt was reacted with cyclopropylamine in toluene to form amide I which was methylated with MeI using lithium pyrrolidide in THF to form amide II (R = cyclopropylamino). The methylated amide was converted to the ammonium salt II (R = ONH4) with NaOH and MeOH, which was subsequently transformed to simvastatin by stirring in toluene at 105°. Preparation of simvastatin starting from lovastatin was also presented.

IT 79902-63-9P

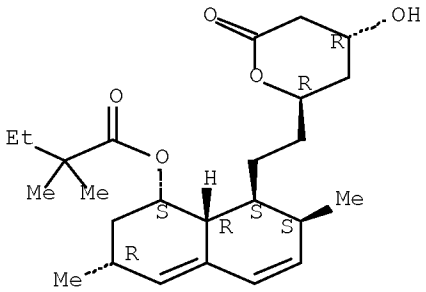
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)

(preparation of simvastatin from lovastatin or mevinolinic acid)

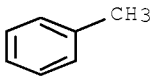
RN 79902-63-9 HCAPLUS

CN Butanoic acid, 2,2-dimethyl-, (1S,3R,7S,8S,8aR)-1,2,3,7,8,8a-hexahydro-3,7-dimethyl-8-[2-[(2R,4R)-tetrahydro-4-hydroxy-6-oxo-2H-pyran-2-yl]ethyl]-1-naphthalenyl ester (CA INDEX NAME)

Absolute stereochemistry.

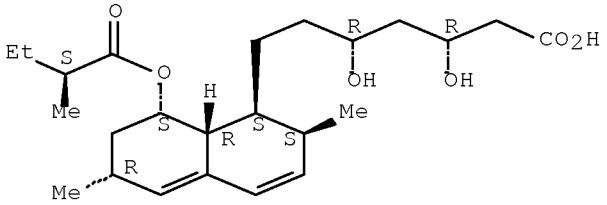


IT 108-88-3, uses
RL: NUU (Other use, unclassified); USES (Uses)
(preparation of simvastatin from lovastatin or mevinolinic acid)
RN 108-88-3 HCAPLUS
CN Benzene, methyl- (CA INDEX NAME)



IT 75225-51-3
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of simvastatin from lovastatin or mevinolinic acid)
RN 75225-51-3 HCAPLUS
CN 1-Naphthaleneheptanoic acid, 1,2,6,7,8,8a-hexahydro-β,δ-dihydroxy-2,6-dimethyl-8-[(2S)-2-methyl-1-oxobutoxy]-, (βR,δR,1S,2S,6R,8S,8aR)- (CA INDEX NAME)

Absolute stereochemistry.



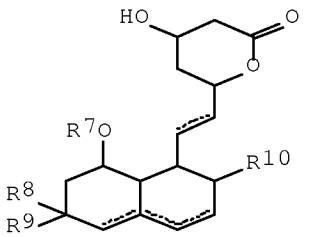
REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

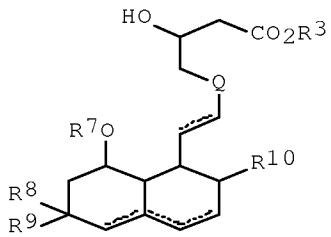
L99 ANSWER 8 OF 10 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1994:245504 HCAPLUS Full-text
DOCUMENT NUMBER: 120:245504
TITLE: Preparation of phosphorus containing alkynyl derivatives useful as intermediates in the preparation of keto phosphonates and mevinolinic acid derivatives

INVENTOR(S): Todd, Richard Simon; Reeve, Maxwell; Davidson, Alan Hornsby
PATENT ASSIGNEE(S): British Bio-Technology Ltd., UK
SOURCE: PCT Int. Appl., 28 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9322321	A1	19931111	WO 1993-GB837	19930422
W: AU, CA, FI, HU, JP, KR, NO, NZ, PT, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9342655	A	19931129	AU 1993-42655	19930422
PRIORITY APPLN. INFO.:			GB 1992-8790 A	19920423
			WO 1993-GB837 A	19930422

OTHER SOURCE(S): CASREACT 120:245504; MARPAT 120:245504
GI


II


III

AB Compds. of general formula R1R2P(O)nC.tplbond.CCH2-Y-CH2-X (I) [n = 0 or 1; R1, R2 each independently represents R, OR, NHR or NR2 in which the two R groups may be the same of different and wherein: R is (halo-substituted)C1-8 alkyl , C2-8 alkenyl, C3-8 cycloalkyl, C1-6 alkyl-O-C1-6 alkyl, C1-8 alkyl(C3-8 cycloalkyl), Ph, C1-C6 alkylphenyl, C2-C6-alkenylphenyl, or R1R2 together form a C2-C6 alkyl bridge optionally substituted at any position with a C1-4 alkyl group; Y is CHOH, CHOQ where Q is a suitable protecting group or C:O; X represents any group which does not interact chemical or sterically with the group Y] are prepared as useful intermediates in the preparation of ketophosphonates and their derivs. and these, in turn, are useful synthetic intermediates for a variety of compds., e.g., mevinolinic acid derivs. Compds. I are prepared by reaction of R1R2P(O)nC.tplbond.CR5 (R5 = protecting group) with A-CH2-Y-CH2-X (A = leaving group or Y and A together form -CHO- or -CHOSO2-O- bridges) under basic conditions. Compds. R1R2P(O)nCH2C(O)CH2-Y-CH2-X are prepared by reaction of compds. I with an aqueous acid under catalytic conditions in an alc. solvent [e.g., Hg(II) salt catalyst, aqueous H2SO4, in MeOH]. Thus, treatment of di-Et acetylenephosphonate with BuLi in THF, then reaction with BF3.Et2O and Me (S)-3,4-epoxybutanoate afforded 25% Me (S)-6-(diethylphosphono)-3-hydroxyhex-5-ynoate which was converted to Me (S)-6-(diethylphosphono)-3-hydroxyhex-5-oxohexanoate (83% yield, HgSO4 catalyst, with aqueous H2SO4 in MeOH). The latter was then reacted to give a derivative of mevolinic acid. The preparation of mevolinic acid derivs. II and III [R7 = H, C(O)C1-8 alkyl, etc., R8 = H, C1-8 alkyl etc., R9 = H, C1-8 alkyl, R10 = H,

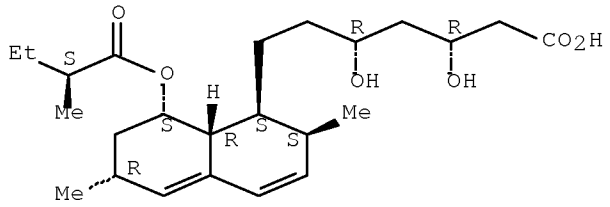
Me, Et, all dashed lines represent single or double bonds] via the keto phosphonates are also claimed.

IT 75225-51-3DP, Mevinolinic acid, derivs.
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, via keto phosphonates)

RN 75225-51-3 HCAPLUS

CN 1-Naphthaleneheptanoic acid, 1,2,6,7,8,8a-hexahydro-β,δ-dihydroxy-2,6-dimethyl-8-[(2S)-2-methyl-1-oxobutoxy]-, (βR,δR,1S,2S,6R,8S,8aR)- (CA INDEX NAME)

Absolute stereochemistry.



L99 ANSWER 9 OF 10 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1990:233955 HCAPLUS Full-text
DOCUMENT NUMBER: 112:233955
TITLE: Hollow fiber solvent extraction of pharmaceutical products: a case study
AUTHOR(S): Prasad, R.; Sirkar, K. K.
CORPORATE SOURCE: Dep. Chem. Chem. Eng., Stevens Inst. Technol., Hoboken, NJ, 07030, USA
SOURCE: Journal of Membrane Science (1989), 47(3), 235-59
CODEN: JMESDO; ISSN: 0376-7388
DOCUMENT TYPE: Journal
LANGUAGE: English

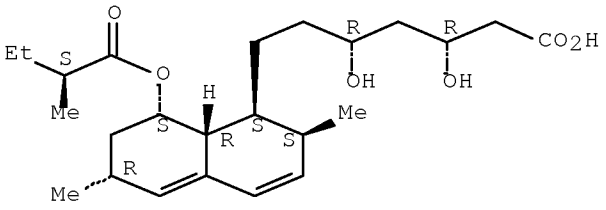
AB Dispersion-free solvent extraction using Celgard microporous hydrophobic hollow fibers and flat membranes was utilized for extraction/purification of fermentation-based pharmaceutical products. Extraction as well as back extraction was studied using a pH swing procedure. Problems of emulsion formation, inherent in current processes, were avoided to obtain stable dispersion-free operation. Very high solute recoveries and mass transfer rates were obtained in the hollow fiber devices. Modular plant design using a series-parallel arrangement of this type of extractors and cost of existing dispersion-based devices indicate that these novel devices can compete effectively with com. extractors.

IT 75225-51-3P, MK 819
RL: PREP (Preparation)
(hollow-fiber solvent extraction in purification of)

RN 75225-51-3 HCAPLUS

CN 1-Naphthaleneheptanoic acid, 1,2,6,7,8,8a-hexahydro-β,δ-dihydroxy-2,6-dimethyl-8-[(2S)-2-methyl-1-oxobutoxy]-, (βR,δR,1S,2S,6R,8S,8aR)- (CA INDEX NAME)

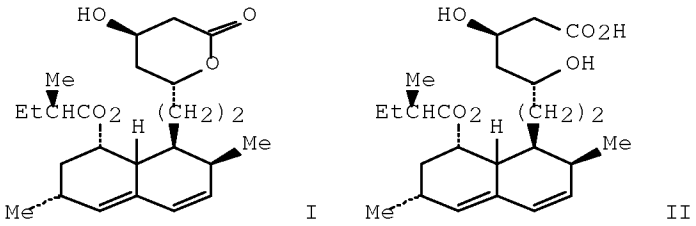
Absolute stereochemistry.



L99 ANSWER 10 OF 10 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1982:422084 HCAPLUS Full-text
DOCUMENT NUMBER: 97:22084
ORIGINAL REFERENCE NO.: 97:3865a,3868a
TITLE: Ammonium salt of hypocholesteremic fermentation product
INVENTOR(S): Albers-Schonberg, George
PATENT ASSIGNEE(S): Merck and Co., Inc. , USA
SOURCE: U.S., 12 pp. Cont.-in-part of U.S. Ser. No. 159,983. CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 4319039	A	19820309	US 1980-176816	19800811
US 4231938	A	19801104	US 1979-48946	19790615
US 4342767	A	19820803	US 1980-159983	19800616
PRIORITY APPLN. INFO.:			US 1979-48946 A2	19790615
			US 1980-114459 A2	19800123
			US 1980-159983 A3	19800616

OTHER SOURCE(S): CASREACT 97:22084
GI



I II

AB Hypocholesteremic products I [75330-75-5] and II [75225-51-3] are obtained by cultivation of Aspergillus. In addition, the salts and esters of I and II are prepared Thus, a preculture of Aspergillus species MF-4833 was inoculated into a pH 7.3 medium containing tomato paste 20, primary yeast 10, CPC starch 20 g, and 5 mg CoCl2.6H2O/L and incubated for 11 days at 28° without agitation. The broth filtrate (10.2 L) was extracted with EtOAc and the solids by MeOH. The solid residues from these extns. were dissolved in MeOH

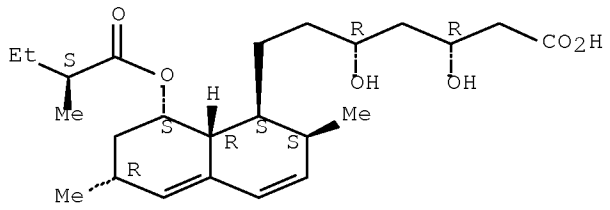
and fractionated into 3 fractions. The fraction with the highest activity was filtered through a bed of Waters Bondapak C18/Porasil B and eluted with MeOH and the eluate concentrated Repeated chromatog. on a Waters μC18 column with MeOH-0.05M ammonium phosphate as the developing solvent produced fractions, with those absorbing at 236 nm combined and concentrated under reduced pressure. After adjusting the pH of the concentrate to 6.2, it was extracted with EtOAc, the organic layer was dried and concentrated to dryness, and the residue dissolved in MeOH. Repeating the chromatog. of the MeOH solution gave eluates which were combined with previously obtained eluates, concentrated to an aqueous solution, and extracted with CHCl3. After dissolving the CHCl3 residue in MeOH and evaporating to dryness, 3.5 mg II was obtained. Cuts containing I were combined and extracted with CHCl3, yielding, after drying, 0.87 mg I.

IT 75225-51-3
RL: BIOL (Biological study)
(from Aspergillus, as hypocholesteremic)

RN 75225-51-3 HCAPLUS

CN 1-Naphthaleneheptanoic acid, 1,2,6,7,8,8a-hexahydro-β,δ-dihydroxy-2,6-dimethyl-8-[(2S)-2-methyl-1-oxobutoxy]-, (βR,δR,1S,2S,6R,8S,8aR)- (CA INDEX NAME)

Absolute stereochemistry.

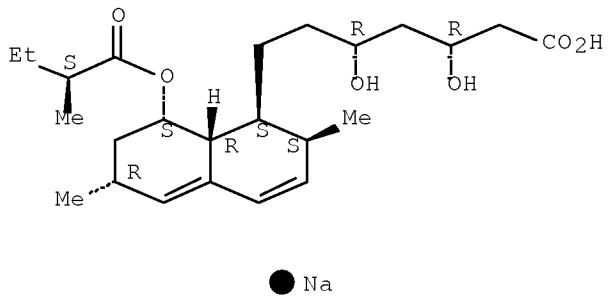


IT 75225-50-2P 77550-67-5P
RL: BMF (Bioindustrial manufacture); BIOL (Biological study); PREP (Preparation)
(manufacture of)

RN 75225-50-2 HCAPLUS

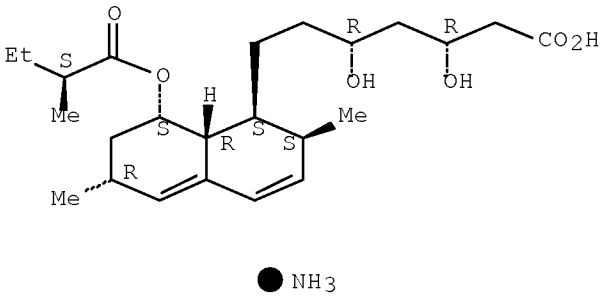
CN 1-Naphthaleneheptanoic acid, 1,2,6,7,8,8a-hexahydro-β,δ-dihydroxy-2,6-dimethyl-8-[(2S)-2-methyl-1-oxobutoxy]-, monosodium salt, (βR,δR,1S,2S,6R,8S,8aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

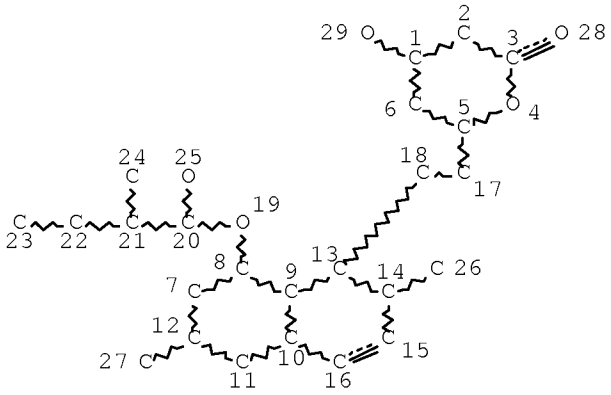


RN 77550-67-5 HCAPLUS
CN 1-Naphthaleneheptanoic acid, 1,2,6,7,8,8a-hexahydro-β,δ-dihydroxy-2,6-dimethyl-8-[(2S)-2-methyl-1-oxobutoxy]-, ammonium salt (1:1), (βR,δR,1S,2S,6R,8S,8aR)- (CA INDEX NAME)

Absolute stereochemistry.



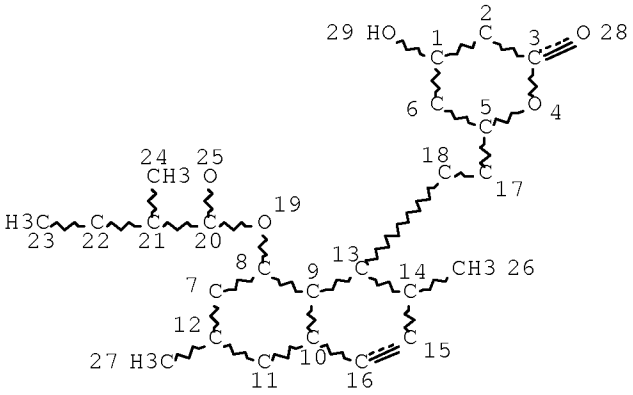
=> => D STAT QUE L100
L56 STR



NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 29

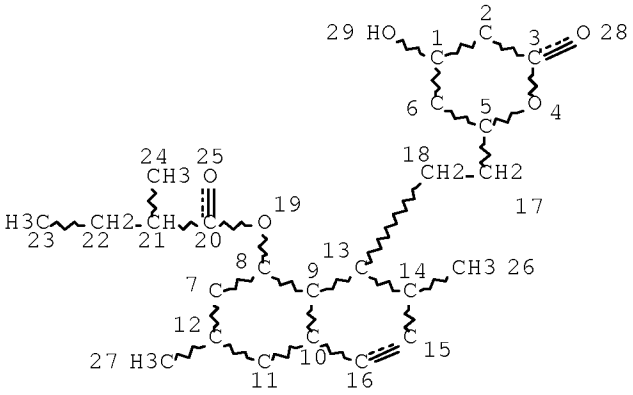
STEREO ATTRIBUTES: NONE
L58 336 SEA FILE=REGISTRY SSS FUL L56
L59 STR



NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 29

STEREO ATTRIBUTES: NONE
L60 145 SEA FILE=REGISTRY SUB=L58 SSS FUL L59
L61 STR



NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 29

STEREO ATTRIBUTES: NONE
L63 SCR 2127
L64 33 SEA FILE=REGISTRY SUB=L58 SSS FUL L61 NOT L63
L65 3561 SEA FILE=HCAPLUS ABB=ON PLU=ON L64
L66 1 SEA FILE=REGISTRY ABB=ON PLU=ON "MEVINOLINIC ACID"/CN
L67 SEL PLU=ON L66 1- CHEM : 10 TERMS

```
L68          162 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L67
L69          164 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L68 OR MEVINOLINIC(W)ACID OR
                 MEVINOLINATE
L70          119 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L65 AND L69
L71        18338 SEA FILE=HCAPLUS ABB=ON  PLU=ON  ("FERMENTATION (L) BROTH"/CV
                 OR "BROTH FERMENTATION"/CV) OR FERMENTATION(L)(BROTH OR MEDIA)
L72           13 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L69(L)L71
L74          328 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L65(L)(BMF OR PREP OR BPN)/RL

L75           30 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L70 AND L74
L79           18 SEA FILE=REGISTRY ABB=ON  PLU=ON  MINERAL(L)ACID OR SULFONIC
                 ACID/CN OR NITRIC ACID/CN OR ORTHOPHOSPHORIC ACID/CN OR
                 HYDROCHLORIC ACID/CN
L80            1 SEA FILE=REGISTRY ABB=ON  PLU=ON  ORTHOPHOSPHORIC ACID/CN
L81        72933 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L80
L82       399316 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L79 OR (MINERAL OR SULFURIC
                 OR NITRIC OR L81 OR HYDROCHLORIC)(W) ACID
L83           15 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L74 AND L82
L84         1388 SEA FILE=REGISTRY ABB=ON  PLU=ON  SOLVENT OR SOLVENTS OR
                 HYDROCARBONS/CN
L86      1959522 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L83 OR L84 OR SOLVENT OR
                 HYDROCARBON OR ?DICHLOROMETHANE OR CHLOROFORM OR ISOPROPANOL
                 OR ALUMINA OR ACETONE
L87          233 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L65 AND L86
L88           48 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L87 AND L74
L89           80 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L65 AND (FILT? OR ?CRYSTALI?
                 OR EVAPORA?)
L90           29 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L89 AND L74
L91           45 SEA FILE=HCAPLUS ABB=ON  PLU=ON  (L83 OR L88 OR L90) NOT L75
L92          112 SEA FILE=REGISTRY ABB=ON  PLU=ON  L60 NOT L64
L93          133 SEA FILE=REGISTRY ABB=ON  PLU=ON  L92 OR LOVASTATIN
L94         6902 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L93 OR LOVASTATIN
L95          462 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L94(L)(BMF OR PREP OR BPN)/RL

L97           60 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L95 AND L69
L98           23 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L97 AND L86
L99           10 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L98 NOT (L75 OR L91)
L100           3 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L72 NOT (L75 OR L91 OR L99)


=> D IBIB ABS HITSTR L100 1-3

L100 ANSWER 1 OF 3  HCAPLUS  COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER:        2007:1460526  HCAPLUS  Full-text
TITLE:                   Determination of lovastatin and lovastatin acid in
                         fermentation broth by HPLC
AUTHOR(S):               Feng, Jianli; Xu, Zhenliang; Wang, Xuejun; Yang,
                         Zuoguo
CORPORATE SOURCE:        Chemical Engineering Research Center, East China
                         University of Science and Technology, Shanghai,
                         200237, Peop. Rep. China
SOURCE:                  Zhongguo Yiyao Gongye Zazhi (2006), 37(7), 494-495
                         CODEN: ZYGZEA; ISSN: 1001-8255
PUBLISHER:               Zhongguo Yiyao Gongye Zazhi Bianjibu
DOCUMENT TYPE:           Journal
LANGUAGE:                Chinese
AB    A HPLC method was established for the determination of lovastatin and
      lovastatin acid in the fermentation broth.  A C8 column was used with the
```

mobile phase of 10 mmol/L phosphoric acid-acetonitrile (40:60), at the detection wavelength of 238 nm. The calibration curves of lovastatin and lovastatin acid were linear in the ranges of 0.012-0.096 mg/mL and 0.01-0.08 mg/mL, resp. The average recoveries were 99.8% and 98.7%, resp.

L100 ANSWER 2 OF 3 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1995:608698 HCAPLUS Full-text
DOCUMENT NUMBER: 123:31295
TITLE: High-performance liquid chromatographic analysis of mevinolin as mevinolinic acid in fermentation broths
AUTHOR(S): Friedrich, Jozica; Zuzek, Mateja; Bencina, Mojca; Cimerman, Aleksa; Strancar, Ales; Radez, Ivan
CORPORATE SOURCE: National Institute of Chemistry, Hajdrihova 19, Ljubljana, 61115, Slovenia
SOURCE: Journal of Chromatography, A (1995), 704(2), 363-7
CODEN: JCRAEY; ISSN: 0021-9673
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English

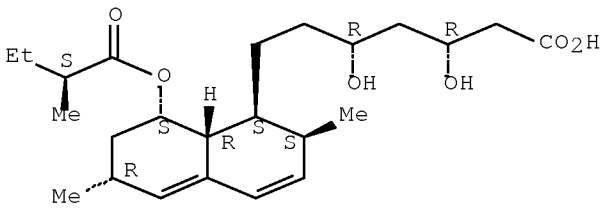
AB High-performance liquid chromatog. anal. of mevinolin in fermentation broth was initially performed after addition of acid and extraction with methanol using a mobile phase at pH 3.0. Under such conditions, mevinolin was present in three different forms: as a lactone, as the corresponding β-hydroxy acid (mevinolinic acid) and as its Me ester. To achieve accurate and reproducible results, the method was modified such that only one form was present: mevinolinic acid. The fermentation broth samples were adjusted to pH 7.7 before the extraction with methanol, and the pH of the mobile phase was adjusted to 7.7 as well. For the separation a 250 × 4 mm I.D. column, thermostated at 40℃ and packed with Spherisorb ODS 2 of 5 μm particle size, was used. Under these conditions, mevinolin was detected at 237 nm as a single peak of a β-hydroxy acid, which has the lowest retention time of all three forms.

IT 75225-51-3, Mevinolinic acid
RL: ANT (Analyte); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(high-performance liquid chromatog. anal. of mevinolin as mevinolinic acid in fermentation broths)

RN 75225-51-3 HCAPLUS

CN 1-Naphthaleneheptanoic acid, 1,2,6,7,8,8a-hexahydro-β,δ-dihydroxy-2,6-dimethyl-8-[(2S)-2-methyl-1-oxobutoxy]-, (βR,δR,1S,2S,6R,8S,8aR)- (CA INDEX NAME)

Absolute stereochemistry.

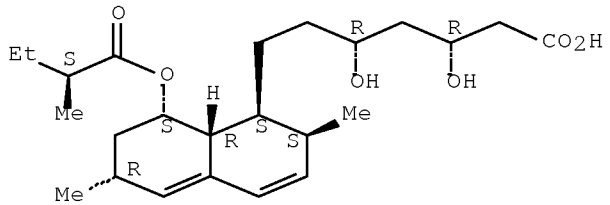


L100 ANSWER 3 OF 3 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1993:426708 HCAPLUS Full-text
DOCUMENT NUMBER: 119:26708
TITLE: Determination of Lovastatin (mevinolin) and mevinolinic acid in fermentation liquids
AUTHOR(S): Kysilka, Roman; Kren, Valdimir
CORPORATE SOURCE: Watrex Inst., Prague, 169 00, Czech.
SOURCE: Journal of Chromatography (1992), 630(1-2), 415-17
CODEN: JOCRAM; ISSN: 0021-9673
DOCUMENT TYPE: Journal
LANGUAGE: English

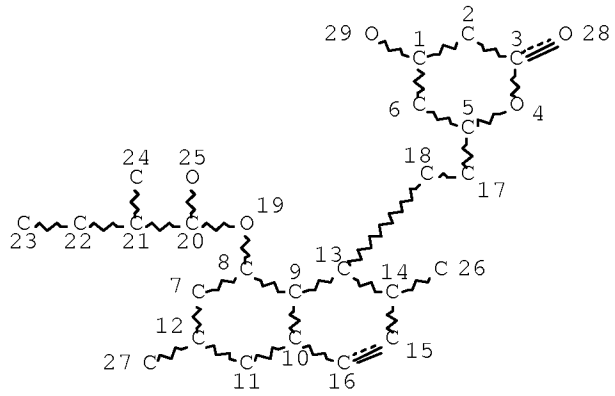
AB A rapid and simple HPLC method is described for the determination of Lovastatin and mevinolinic acid in fermentation fluids of Aspergillus terreus using a Separon SGX C18 column and MeOH–18 mM H3PO4 (77.5:22.5, volume/volume) as mobile phase with detection at 238 nm. The detection limits of Lovastatin and mevinolinic acid were 20–30 ng/mL.

IT 75225-51-3, Mevinolinic acid
RL: ANT (Analyte); ANST (Analytical study)
(determination of, in fermentation broth by HPLC)
RN 75225-51-3 HCAPLUS
CN 1-Naphthaleneheptanoic acid, 1,2,6,7,8,8a-hexahydro-β,δ-dihydroxy-2,6-dimethyl-8-[(2S)-2-methyl-1-oxobutoxy]-, (βR,δR,1S,2S,6R,8S,8aR)- (CA INDEX NAME)

Absolute stereochemistry.



=> => D STAT QUE L107
L56 STR

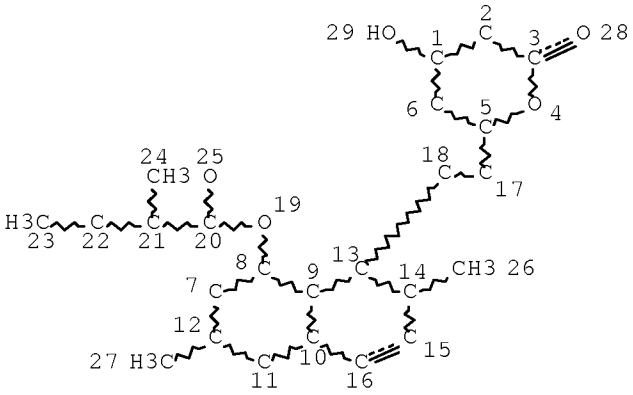


NODE ATTRIBUTES:

DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 29

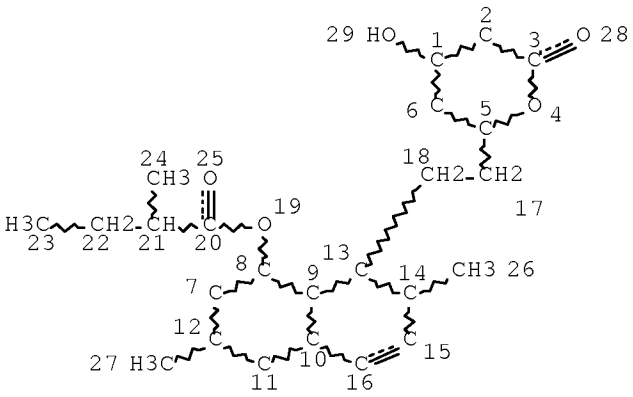
STEREO ATTRIBUTES: NONE
L58 336 SEA FILE=REGISTRY SSS FUL L56
L59 STR



NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 29

STEREO ATTRIBUTES: NONE
L60 145 SEA FILE=REGISTRY SUB=L58 SSS FUL L59
L61 STR



NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

```
GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS  29

STEREO ATTRIBUTES: NONE
L63             SCR 2127
L64          33 SEA FILE=REGISTRY SUB=L58 SSS FUL L61 NOT L63
L65        3561 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L64
L66           1 SEA FILE=REGISTRY ABB=ON  PLU=ON  "MEVINOLINIC ACID"/CN
L67             SEL  PLU=ON  L66 1- CHEM :      10 TERMS
L68         162 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L67
L69         164 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L68 OR MEVINOLINIC(W)ACID OR
                MEVINOLINATE
L70         119 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L65 AND L69
L71       18338 SEA FILE=HCAPLUS ABB=ON  PLU=ON  ("FERMENTATION (L) BROTH"/CV
                OR "BROTH FERMENTATION"/CV) OR FERMENTATION(L)(BROTH OR MEDIA)
L74         328 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L65(L)(BMF OR PREP OR BPN)/RL

L75          30 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L70 AND L74
L76        8124 SEA FILE=HCAPLUS ABB=ON  PLU=ON  LACTONIZATION/CV OR ?LACTONIZA
                TION OR ?LACTONISATION
L79          18 SEA FILE=REGISTRY ABB=ON  PLU=ON  MINERAL(L)ACID OR SULFONIC
                ACID/CN OR NITRIC ACID/CN OR ORTHOPHOSPHORIC ACID/CN OR
                HYDROCHLORIC ACID/CN
L80           1 SEA FILE=REGISTRY ABB=ON  PLU=ON  ORTHOPHOSPHORIC ACID/CN
L81       72933 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L80
L82      399316 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L79 OR (MINERAL OR SULFURIC
                OR NITRIC OR L81 OR HYDROCHLORIC)(W) ACID
L83          15 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L74 AND L82
L84        1388 SEA FILE=REGISTRY ABB=ON  PLU=ON  SOLVENT OR SOLVENTS OR
                HYDROCARBONS/CN
L86     1959522 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L83 OR L84 OR SOLVENT OR
                HYDROCARBON OR ?DICHLOROMETHANE OR CHLOROFORM OR ISOPROPANOL
                OR ALUMINA OR ACETONE
L87         233 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L65 AND L86
L88          48 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L87 AND L74
L89          80 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L65 AND (FILT? OR ?CRYSTALI?
                OR EVAPORA?)
L90          29 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L89 AND L74
L91          45 SEA FILE=HCAPLUS ABB=ON  PLU=ON  (L83 OR L88 OR L90) NOT L75
L92         112 SEA FILE=REGISTRY ABB=ON  PLU=ON  L60 NOT L64
L93         133 SEA FILE=REGISTRY ABB=ON  PLU=ON  L92 OR LOVASTATIN
L94        6902 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L93 OR LOVASTATIN
L95         462 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L94(L)(BMF OR PREP OR BPN)/RL

L97          60 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L95 AND L69
L98          23 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L97 AND L86
L99          10 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L98 NOT (L75 OR L91)
L101        458 SEA FILE=HCAPLUS ABB=ON  PLU=ON  ("KUMAR SANJAY"/AU OR "KUMAR
                SANJAY RAI"/AU OR "KUMAR SANJAY S"/AU OR "KUMAR SANJAY
                SANTH"/AU) OR VAISHNAV SANJAY KUMAR/AU
L102         13 SEA FILE=HCAPLUS ABB=ON  PLU=ON  THAKUR B/AU OR THAKUR
                BHUPENDRA HARISHCHANDRA/AU
L103         10 SEA FILE=HCAPLUS ABB=ON  PLU=ON  KADAM S/AU OR KADAM S R/AU OR
                KADAM SUBHASH R?/AU
L104          1 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L101 AND (L102 OR L103)
L105          1 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L102 AND L103
L106          3 SEA FILE=HCAPLUS ABB=ON  PLU=ON  (L101 OR L102 OR L103) AND
```

(L65 OR L68 OR L71 OR L76 OR L94)
L107 2 SEA FILE=HCAPLUS ABB=ON PLU=ON (L104 OR L105 OR L106) NOT (L75 OR L91 OR L99)

=> D IBIB ABS HITSTR L107 1-2

L107 ANSWER 1 OF 2 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:902391 HCAPLUS Full-text
DOCUMENT NUMBER: 145:470034
TITLE: Production of lactic acid and fructose from media with cane sugar using mutant of Lactobacillus delbrueckii NCIM 2365
AUTHOR(S): Patil, S. S.; Kadam, S. R.; Bastawde, K. B.; Khire, J. M.; Gokhale, D. V.
CORPORATE SOURCE: National Chemical Laboratory, NCIM Resource Centre, Maharashtra, India
SOURCE: Letters in Applied Microbiology (2006), 43(1), 53-57
CODEN: LAMIE7; ISSN: 0266-8254
PUBLISHER: Blackwell Publishing Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB To examine the potential of Lactobacillus delbrueckii mutant, Uc-3 to produce lactic acid and fructose from sucrose-based media. The mutant of L. delbrueckii NCIM 2365 was cultivated in shake flask containing hydrolyzed cane sugar (sucrose)-based medium. The lactic acid yield and volumetric productivity with hydrolyzed cane concentration up to 200 g l-1 were in the range of 92-97% of the theor. value and between 2.7 and 3.8 g l-1 h-1, resp. The fructose fraction of the syrup produced was more than 95% when the total initial sugar concentration in the medium was higher (150-200 g l-1). There are no unwanted byproducts detected in the fermentation broth. We demonstrated that L. delbrueckii mutant Uc-3 was able to utilize glucose preferentially to produce lactic acid and fructose from hydrolyzed cane sugar in batch fermentation process. These findings will be useful in the production of lactic acid and high fructose syrups using media with high concns. of sucrose-based raw materials. This approach can lead to modification of the traditional fermentation processes to obtain value-added byproducts, attaining better process economics.
REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L107 ANSWER 2 OF 2 HCAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:796164 HCAPLUS Full-text
DOCUMENT NUMBER: 145:230465
TITLE: Process for manufacture of simvastatin
INVENTOR(S): Kadam, Subhash Rajaram; Patil, Mahendra Raghunath; Patil, Madhukar Shaligram; Sasane, Sachin Arun
PATENT ASSIGNEE(S): Lupin Limited, India
SOURCE: PCT Int. Appl., 28pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006082594	A1	20060810	WO 2005-IN208	20050617

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

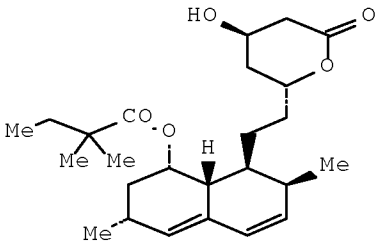
IN 2005MU00116	A	20060915	IN 2005-MU116	20050204
AU 2005326565	A1	20060810	AU 2005-326565	20050617
EP 1848706	A1	20071031	EP 2005-799252	20050617

R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, HR, MK

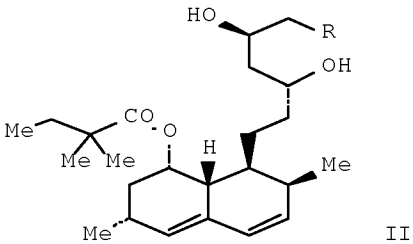
PRIORITY APPLN. INFO.: IN 2005-MU116 A 20050204
WO 2005-IN208 W 20050617

OTHER SOURCE(S): CASREACT 145:230465

GI



I



II

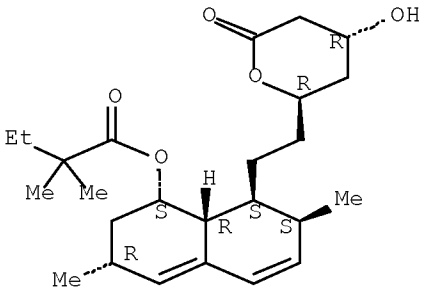
AB An improved method was disclosed for the manufacture of simvastatin (I) in high purity. The process comprised agitating an open-chain acid derivative II (R = CO2H, CO2-.NH4+, CO2M, M = alkali metal) in an organic solvent and in an inert atmospheric at a temperature of between 27° to 40° in the presence of a weak acid followed by neutralization with an organic base and obtaining the desired simvastatin in high purity and substantially free of impurities through a step of isolation and crystallization

IT 79902-63-9P, Simvastatin
RL: IMF (Industrial manufacture); PUR (Purification or recovery); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(process for the preparation and purification of simvastatin)

RN 79902-63-9 HCAPLUS

CN Butanoic acid, 2,2-dimethyl-, (1S,3R,7S,8S,8aR)-1,2,3,7,8,8a-hexahydro-3,7-dimethyl-8-[2-[(2R,4R)-tetrahydro-4-hydroxy-6-oxo-2H-pyran-2-yl]ethyl]-1-naphthalenyl ester (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=>